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ORIGINAL ARTICLE.

THE COMPARATIVE RARITY OF PULMONARY TUBERCULOSIS IN THE HIGHLANDS OF PENNSYLVANIA AND THE ADJACENT COUNTIES OF NEW YORK.[1]

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IF the profession were asked what district in the New England or Middle States showed the greatest immunity from pulmonary tuberculosis, the answer would probably be "The Adirondack Mountains." Without, however, disparaging that great health-resort, where such remarkable opportunities for pleasure and recuperation are afforded to the tens of thousands that flock there—a resort to which I am personally deeply attached—I would, nevertheless, call attention to a region much nearer the homes of many of us; in most respects more suitable for continuous residence, and apparently even more healthful than the Adirondack region itself.

The district referred to falls partly within the State of New York and partly within Pennsylvania. The seven counties along the southern border of New York are Chautauqua, Cattaraugus, Allegany, Steuben, Chemung, Tioga, and Broome. The neighboring region in northern Pennsylvania includes the counties of McKean, Potter, Forest, Clarion, Elk, Cameron, Union, and Sullivan, and at some distance to the eastward, Pike County. In all of this region, comprising over 12,000 square miles, nearly equally divided between New York and Pennsylvania (6545 miles in New York, 5557 in Pennsylvania), there is, according to the best available information, a population of over 1000 persons to each annual death from pulmonary tuberculosis. I confess I was somewhat surprised to discover that in New York State the southern tier of counties from Broome westward make the best returns.

Taking the reports of the State Board of Health for 1893, I find that in the maritime district, including New York, Westchester County, and Long Island, there are 400 persons living for every annual death from pulmonary tuberculosis; in the Hudson River district, 550. Next in order comes the Mohawk Valley; then the Lake Ontario and western region; next the central counties; then the Adirondack and northern district, in which there are from 854 to 985 persons living to one death from pulmonary tuberculosis; and finally and best of all, in New York the seven counties of the southern tier, with 1091 persons living to each death from pulmonary tuberculosis. The accompanying map shows this relative prevalence of pulmonary tuberculosis in the State of New York.

During each of the last four years the mortality from pulmonary tuberculosis in the southern tier of counties in New York, in comparison with the total deaths, is far below what obtains in other portions of the State. This is clearly illustrated by the annexed chart. It is evident that from whatever standpoint we look at the subject, the southern tier of counties are the freest from pulmonary tuberculosis.

Among the characteristics of this region are the following:

Population. Sixty-two persons per square mile; engaged chiefly in agriculture.

Soil. Highly productive. Geologic formation, limestone and sandstone.

Products. Hay, oats, potatoes, grapes, standing timber.

Temperature. The mean annual temperature in 1892 was 44.5°, or six and one-half degrees less than in New York City, and three and one-half degrees more than in the Adirondack region. The latest killing frost occurred on April 26th at Jamestown, and the first frost November 5th; this was about the same as in New York, and gave an agricultural season twenty-four days longer than in the Adirondack region.[1]

Rainfall. This varies from 37 to 47 inches annually in the southern tier. The amount is usually less than in other portions of the State.

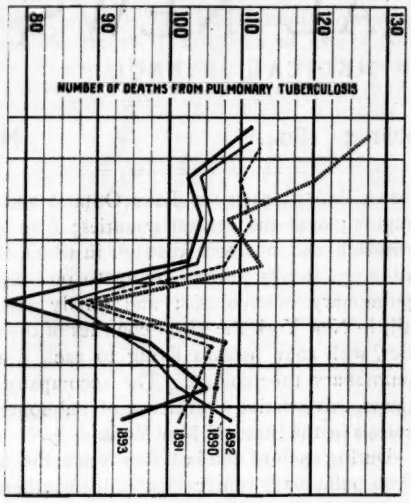
Elevation. In the southern tier of counties the following elevations are noted:

Alfred Center, 1820 feet; Angelica, 1340 feet; Friendship, 1550 feet; Binghamton, 860 feet; Nineveh, 1032 feet; Humphrey, 1500 feet; Sher-

[1] Read at the annual meeting of the American Climatological Association at Washington, D. C., June 1, 1894.

[1] The stations in the southern tier district reckoned were Jamestown, 47°; Alfred Centre, 43°; Angelica, 43°; South Canisteo, 43°; Addison, 45°; Hammondsport, 43°; Binghamton, 54°; Humphrey, 50°.

In the Adirondack district the stations are Lyon Mountain, 39.2°; Malone, 41°; "Number Four," 40°; and stations in Essex and St. Lawrence counties, 42°.



IN EACH 1000 DEATHS FROM ALL CAUSES.

MARITIME DISTRICT.
Population, 3,200,950—per cent. city population, 87.17.

HUDSON VALLEY DISTRICT.
Population, 684,268—per cent. city population, 40.31.

ADIRONDACK AND NORTHERN DISTRICT.
Population, 386,680—per cent. city population, 7.50.

MOHAWK VALLEY DISTRICT.
Population, 376,116—per cent. city population, 30 93.

SOUTHERN TIER DISTRICT.
Population, 405,967—per cent. city population, 26.85.

EAST CENTRAL DISTRICT.
Population, 386,600—per cent. city population, 23.75.

WEST CENTRAL DISTRICT.
Population, 311,000—per cent. city population, 12.28.

LAKE ONTARIO AND WESTERN DISTRICT.
Population, 761,756—per cent. city population, 60.60.

man, 1568 feet; Elmira, 863 feet; Savona, 1053 feet.

It will be noted that these elevations are somewhat below those of the stations in the adjacent district in Pennsylvania, to be considered later.

Position with reference to storm-tracks. The region considered is the farthest removed in New York State from the path of greatest frequency of storms. These are prone to pass down the valley of the St. Lawrence. This southern region is thus spared some of the cloud and rain accompanying the moving areas of lowest barometric pressure.

Accessibility and accommodations. All points in this region are reached by the New York, Lake Erie and Western Railroad, and desirable accommodations may be found about Chautauqua Lake and Jamestown.

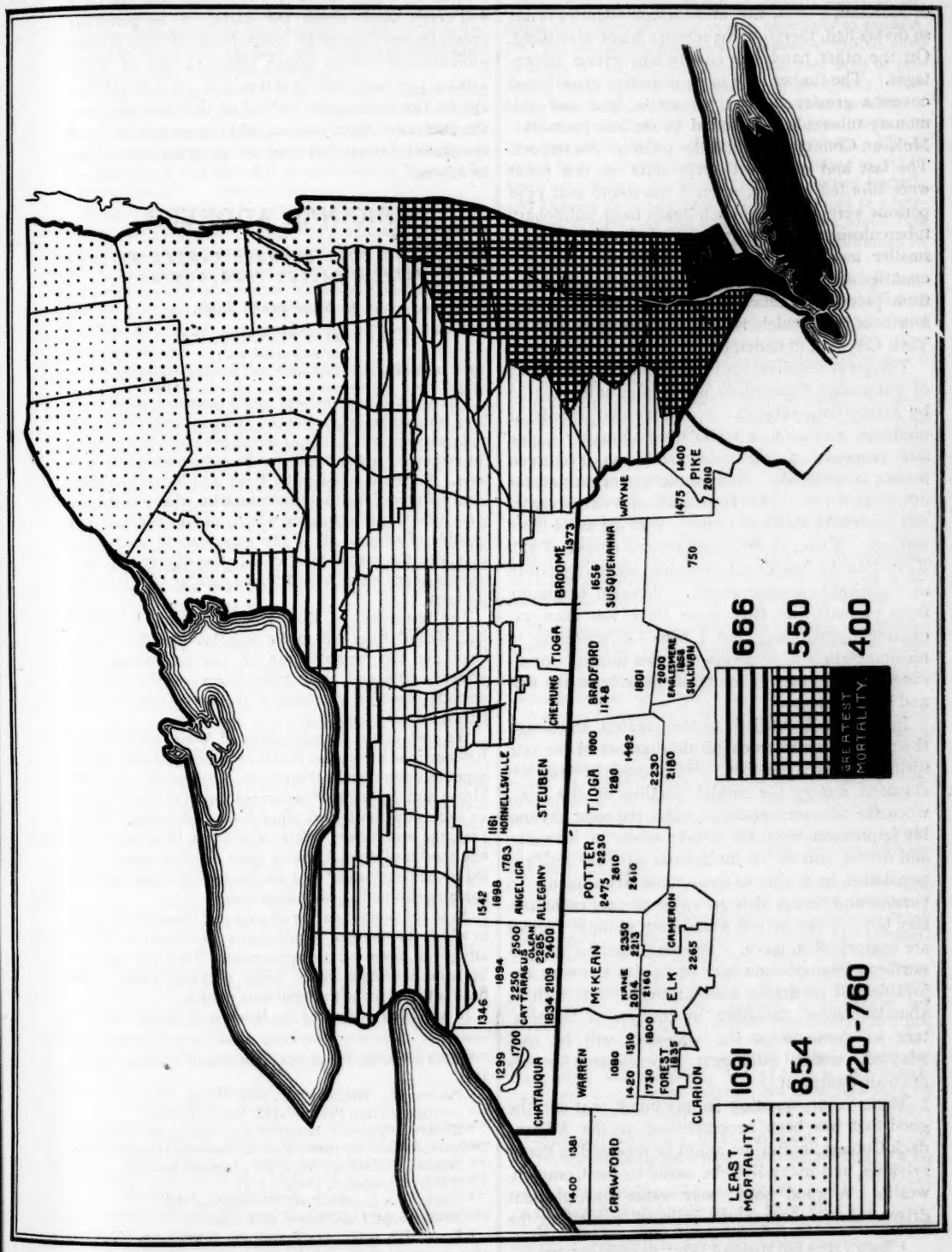
No special claim has been made for this region with reference to the climatic treatment of pulmonary tuberculosis; but in Chautauqua, Cattaraugus, Allegany, and Steuben counties a new and uncontaminated field is opened for the treatment of tuberculous patients, with many opportunities for self-support not found elsewhere.

The Highlands of Pennsylvania adjacent to the New York border are of a somewhat different physical character. The country is wilder, the forests more extensive, the general elevation greater; it is a little cooler, a little drier, a little more primitive. Agriculture is not nearly so remunerative; the industries are more prominently lumbering and mining for coal, iron, and oil. Vast areas of hemlock, and here and there growths of pine cover the mountain-tops, while there are many ridges timbered with beech, birch, and maple. The climate is superb during the months of May, June, July, August, and September; it is distinctly bracing, with the sunshine of more southern latitudes. Cold weather usually sets in about November 1st, and continues in what is called a "solid winter" until the following April. For nearly four months there is usually good sleighing. A temperature of zero is not felt to the same degree as the freezing-point in most places where there is fog, where the air is less dry and bracing, and where the rainfall is greater and the soil more retentive of moisture. Pleurisy and pneumonia are uncommon, and epidemics of diphtheria and scarlet fever are said never to occur. A physician in McKean county writes me: "I have seen but three cases of true diphtheria during my fifteen years' residence here. I have never known a case of pulmonary tuberculosis to originate here, and the cases that come here are greatly benefited or entirely cured."

The broad and high table-land in northwestern Pennsylvania has great topographic advantages over the surrounding region, in that its surface is not so deeply cut by water-courses. The counties of McKean, Forest, Elk, and Clarion comprise the highest ground; the streams take their rise from this "Big Level," as it is called; they are still small and have not produced the deep gullies and narrow valleys which are a common feature throughout northern Pennsylvania.

In the outlying region the chief settlements are necessarily found along these water-courses, while the uninhabited mountain-tops, far above the foggy and fertile valleys, are rarely visited except by lumbermen.

In Sullivan County deep indentations penetrate its entire area; nevertheless, we find on one of the mountain-tops two beautiful lakes, about which are clustered the summer homes of many who have discovered the great benefit to be derived from a



MAP SHOWING THE DISTRIBUTION OF PULMONARY TUBERCULOSIS IN THE STATE OF NEW YORK AND ADJACENT COUNTIES OF PENNSYLVANIA.

The small numerals in the map indicate the altitude; the large figures below, the average number of persons living to each annual death from pulmonary tuberculosis.

residence in this attractive region.[1] The table-land of McKean, Forest, Elk, and Carbon counties is not so diversified, therefore the scenery is not so striking. On the other hand, the county has certain advantages. The timber is of more primitive growth and covers a greater extent; the air is drier and pulmonary tuberculosis is found to be less prevalent. McKean County carries off the palm in this respect. The last and only trustworthy data on this point were afforded in 1880, when it was found that 1330 persons were living to each death from pulmonary tuberculosis during the year. This was a much smaller mortality than obtains in the southern counties of New York (1091 living to each death from pulmonary tuberculosis), and less than one-fourth of that which is annually recorded in New York City and Philadelphia.

The great desideratum in the climatic treatment of pulmonary tuberculosis is a region unfrequented by tuberculous subjects; a country that affords, at moderate elevation, a stimulating climate; a dry and therefore a permeable soil; an evergreen forest; a clear sky, and ample opportunities for out-of-door life. The Highlands of Pennsylvania, and especially McKean County, provide all of these features. Kane, in the southwestern corner of McKean County, has already acquired some reputation as a desirable summer-resort. Personal testimony from patients who have gone there has been exceedingly gratifying, and I have no hesitation in recommending a residence in this locality for all cases of pulmonary tuberculosis in at least the first and second stages.

In order to be utilized to the greatest advantage the patient should reach his destination in the late spring or early summer. He should become acclimated during the milder portion of the year, when the new surroundings make the most favorable impression upon his mind; when in his walks and drives, and in his intercourse with the resident population he is able to form those attachments to persons and things that go so far to incline him to stay beyond the period when most summer visitors are compelled to leave. The fine autumn days in northern Pennsylvania may be to him the most enjoyable and profitable season; the winter, with its abundant snow, unbroken by changes of temperature so common at the seaboard, will be well adapted, under intelligent supervision, for his open-air treatment.

There is no question in my mind that all the good that has been accomplished at the Adirondack Cottage Sanitarium might be repeated in Pennsylvania, and many lives be saved to the Commonwealth. A good hotel, easy walks and pleasant drives, and a convenient railroad constitute the present accommodations; but I hope that the time will come when either the State, in its generous provision for charitable institutions, or else private philanthropy, which seems never to tire of establishing new hospitals in cities, will turn a pitying eye on the tuberculous patient so that he may have the purest air under heaven, and the same skilful and sympathetic treatment that are so generously given to others.

[1] Eagle's Mere and Highland Lake; elevation 2200 feet.

ORIGINAL ADDRESS.

THE PATHOLOGIC CHANGES CAUSED BY CERTAIN SO-CALLED TOXALBUMINS.[1]

An Experimental Study.

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THE crystalline principles called ptomaïns which have been isolated by Selmi, Nencki, Brieger,[2] and others from cultures of bacteria do not, as was once supposed, represent the essentially active agents produced by pathogenic bacteria. Since the isolation by Roux and Yersin[3] in 1888, from cultures of the bacillus diphtheriæ, of an amorphous toxic albuminous substance which, as they showed, was capable of causing all of the symptoms of diphtheria, excepting the pseudo-membrane, other albuminous substances have been obtained from a number of pathogenic bacteria.

The researches of Kobert and Stillmark,[4] Martin,[5] and Hellin[6] have led to the isolation from the castor-bean and the jequirity-bean of two amorphous substances—ricin and abrin respectively—which in many respects resemble the toxic albuminous principles obtained from bacteria.

We owe to the investigations of Weir Mitchell and Reichert[7] the knowledge that the toxicity of snake-venom depends upon certain albuminous constituents, and later Mosso and Springfeld[8] separated from the blood of eels an exquisitely poisonous albuminous substance. Moreover, the well-known effects which the blood-serum of one species of animal exerts upon another species has led to the conclusion[9] that the blood of different animals contains distinctly toxic substances.

As to the precise nature of many of these substances, to which the name of toxalbumins has been provisionally given, there is little agreement. They are regarded by some investigators as being enzymes, while a few deny altogether their albuminous nature.

It has been suggested by Roux and Yersin that the

[1] Read before the Philadelphia Pathological Society, April 26, 1894

[2] Berliner klin. Wochenschrift, 1889, No. 39.

[3] Annales de l'Inst. Pasteur, 1888, No. 12, p. 629

[4] Kobert, Lehrbuch d. Intoxicationen, 1893; also, Kobert and Stillmark, Arbeiten des pathologischen Institutes, Dorpat, 1889, iii.

[5] Martin: Proceedings Royal Soc., London, vol. xlvi.

[6] Hellin: Dissertation, Dorpat, 1891.

[7] Smithsonian Contributions, Washington, 1886.

[8] Rend. Accad. Linc., Rome, 1888, 1889.

[9] Loew: Ein natürliches System der Giftwirkung, München, 1893, p. 79.

diphtheria-toxalbumin is an enzyme, and Stillmark holds the same view concerning ricin, while Nencki[1] considers that the proteids of the blood-serum, to which it is believed by many that animals owe their immunity from disease, belong to the same category.

The recent statement of Brieger and Cohn,[2] based upon the study of the properties of a highly refined tetanus-toxin, that this body, which fails to react with Millon's reagent, and responds to the xantho-proteic test, is not an albumin, is not regarded as sufficient to disprove its proteid nature.[3]

Brieger and Fränkel[4] oppose the view of the enzyme-nature of these bodies; and Fermi,[5] who also objects to this view, considers as militating against it the fact that of 114 described pathogenic microörganisms which produce toxins, only 26 produce proteolytic ferments, and that, on the other hand, of 134 known enzyme-producing bacteria only 25 are pathogenic—that is to say, toxalbumin-producing.[6]

The blood-serum of the dog acts with great energy upon the red blood-corpuscles of the rabbit, and Buchner[7] observed that while the blood-serum of these animals is separately capable of destroying a considerable number of typhoid-bacilli, yet when the serum of the dog and rabbit are mixed, the destructive influence of the mixture upon typhoid-bacilli is less than that possessed by either serum alone. As bearing on this question, the experiments of Robert Hartig[8] on the fungus-parasites of plants are interesting. Thus, while certain of the ferments of this origin dissolve the cellulose of plants and not the intercalated wood-gum, there are others that dissolve the gum and have no effect upon the cellulose. According to Hartig the oak is attacked by ten distinct parasites, each of which produces a different ferment. Two of these dissolve starch—are amylolytic—when acting separately, but when combined they are entirely without action on this substance. Does this not suggest an analogy with the mutual destruction or neutralization of the bactericidal principles of the blood of the rabbit and the dog?

Further, we have grounds for believing that the blood possesses the power of destroying the true ferments, as it does certain of the bacterial products, and, moreover, that the true ferments may act in a manner similar to the vegetable toxalbumins in conferring immunity. Hammersten[9] has shown that if rennet and milk are injected separately into the circulation of rabbits the coagulating influence of the ferment upon the milk is much diminished; and Hildebrand[1] has demonstrated an antiferment in the blood of animals rendered immune to certain of the enzymes, especially to emulsin. He[2] has succeeded, moreover, in rendering rabbits more resistant to the bacillus cuniculicida, and even of protecting them against the organism by previously inoculating them with and making them immune to emulsin.

Heating solutions of many of the toxalbumins or blood-serum to 60° C. destroys their activity. Blood-serum kept for thirty minutes at a temperature of 55° C. loses, according to Buchner, its power to destroy bacteria and likewise its globulicidal action. Exposed to a temperature of 54° C. for the same time I have found that dog's serum is still globulicidal for rabbits, although its activity is diminished.

Blood-serum that has lost its bactericidal and globulicidal properties by being kept at a temperature of 60° C. for thirty minutes has not suffered coagulation, nor have demonstrable optic or chemic changes occurred in it. The lost bactericidal property, it is believed by Emmerich and Tsuboi,[3] can be restored by alkalinization and dialysis, a circumstance that they bring forward as bearing upon the question of the chemic *versus* the vital action of the serum. Buchner,[4] it must be mentioned, disputes the results of Emmerich and Tsuboi and claims that the difference that they observed in the effects of the heated serum before and after alkalinization is explicable on other grounds, as, for example, the alteration in the heated serum as a culture-medium. None of these authors, however, mentions the effect of this treatment upon the globulicidal property of the serum, and to determine this I have made the following experiments:

The blood-serum[5] of a dog, collected after twenty-four hours, was tested as to its toxicity, by injecting 1.5 per cent. of the body-weight into the ear-veins of a rabbit. The animal was profoundly affected, soon manifested hemoglobinuria, and died in ten hours.

A second half-grown rabbit, whose blood-count at 11.15 A.M. was 6,080,000 red corpuscles to the c.mm., received 1 per cent. of its weight of unheated serum. It was dead in five minutes, from thrombosis of the right side of the heart. A second-blood-count, made from the lake-colored blood of the left ventricle taken during the death-struggle, showed 3,872,000 red corpuscles per c.mm.

A third control-rabbit received 1 per cent. of its weight of the same serum heated to 55° C. for one hour, without any effect whatever.

Seventy-five c.cm. of the heated serum were now made alkaline with 7.5 c.cm. of a 3 per cent. solution of pure caustic soda and dialyzed through gut for forty-three hours against seventy-six liters of normal salt-solution. The whole volume of serum now equalled 90 c.cm.

A white-mixed rabbit weighing 1600 grams, whose blood-count on March 21st was 5,664,000, and on March 22d 6,368,000 per c.mm., received at 10.20 A.M. an amount of dialyzed serum which corresponded to 1 per cent. of the body-weight of the original serum (16 c.cm. of the original = 19.5 c.c. of dialyzed serum). No immediate effect was produced. At 11.10 A.M. the blood-count was 4,938,000 per c.mm. No hemoglobinuria or other unfavorable symptom had appeared. On April

[1] Correspondenzblatt für Schweizer Aerzte, 1890.

[2] Zeitschrift für Hygiene, vol. xv, p. 1.

[3] Uschinsky (Centralblatt f. Bakteriologie, Band ix, p. 316) succeeded in cultivating the tetanus-organism in a medium composed of salts and asparagin, and free from albumin. The tetanus-poison obtained from this source still gave the reactions mentioned.

[4] Berliner klin. Wochenschrift, 1890, p. 241.

[5] Archiv für Hygiene, vols. ix and xiv.

[6] Fermi and Pernossi (Zeitschrift f. Hygiene und Infektionskrankheiten, Band xvi, Heft 3, p. 435) believe that they have proved that the enzyme produced by the tetanus-bacillus is distinct from the poison tetanin, and that the latter is not a ferment.

[7] Münchner med. Wochenschrift, 1892.

[8] Lehrbuch der Baumkrankeiten, Berlin, 1882. (Quoted by Loew, ibid.)

[9] Schmidt's Jahrbücher, 1887, Band ccxvi, p. 115.

[1] Virchow's Archiv, vols. cxxi, cxxii, cxxxi.

[2] Hildebrand, Münchener med. Wochenschrift, 1894, No. 15, p. 283.

[3] Centralblatt für Bakteriologie, vols. xii and xiii.

[4] Centralblatt für Bakteriologie, vol. xii, p. 855.

[5] In all cases in which blood-serum was used the drawn blood was placed upon ice immediately after having been obtained.

11th the rabbit was still alive and apparently well, the blood-count on this day showing 5,856,000 per c.mm.

Another rabbit, weighing 1800 grams, whose blood-count on March 21st was 6,112,000 per c.mm., and on March 22d 6,208,000, received at 10.30 A.M., March 22d, 1.5 per cent of its body-weight (27 c.c. of the original = 32.5 c.c. of dialyzed serum) of the dialyzed serum. At 11.25 the blood-count was 5,180,000 per c.mm. At 2 P.M. this rabbit, which appeared perfectly well, received a second quantity of 1.5 per cent. of its body-weight. The blood-count at 3 P.M. showed 4,980,000, and on April 11th, at which time the animal appeared normal, it was 5,952,000.

The second animal, it will be noted, received double the certainly lethal dose of the normal, unheated serum, with relatively slight effect. From these experiments it must be concluded that the globulicidal action of the serum is certainly not entirely restored, and if at all, to a minor degree only, by alkalinization. The animals are still living and so far show no evidence of the toxic effects of the serum. Hence, it would appear that the toxic properties are also lost at this temperature.

In considering the pathologic action of the toxic proteids derived from the several sources mentioned upon susceptible animals we shall find reason to treat of them together. Let us consider for a moment the production of immunity, which, for many bacteria and their products, is such a well-known fact that it need not detain us; and evidence is not wanting for the albumins derived from the higher plants, the phytalbumoses.

Up to the present time no one has succeeded in rendering animals permanently immune to the animal toxic proteids, although Sewell[1] claims to have secured in pigeons an immunity to snake-poison which, however, disappeared after a time.

Ehrlich[2] has shown that mice, which are relatively quite susceptible to ricin and abrin, can be rendered in a high degree immune to the action of these bodies. As concerns ricin, he found that a solution having a concentration of 1 to 750,000, in the quantity of 1 c.c. per 20 grams of weight will often kill mice in from two to four days; and in the same dose a solution of 1 to 200,000 will kill these animals without exception. The local effect of the drug is so intense that it is necessary to resort first to feeding, by which means a low grade of immunity is established, which can then be increased by subcutaneous inoculations. The immunity appears quickly. I have repeated Ehrlich's experiments and have confirmed his results.

For example, two mice were fed with gradually increasing doses for ten days, and at the end of this time an immunity equal to the natural resistance of five, as determined by subcutaneous inoculations with control-animals, was already present. From now on the doses were rapidly increased, so that on the twelfth day the resistance was equal to ten; on the sixteenth, to eighty; on the eighteenth, to one hundred and forty, and on the twentieth day, to two hundred and fifty.

These figures are all low, as the calculation is based on the surely lethal dose of 1 to 250,000, and the highest grade of immunity was not determined. Even at this time the immune animals were found not to be indifferent to the mode of introduction; for of two mice, which up to this point had acted in all respects alike, one was inoculated into the peritoneal cavity, and died in one and a half hours, while the other, after subcutaneous inoculation with the same amount (1 c.c. of a 1 to 1000 solution), became slightly sick, but was perfectly well the next day. The blood of the mouse that succumbed was laky. The blood of immune animals, *i. e.*, in a condition that Ehrlich denominates ricin-proof, contains an antitoxic body, which by simple admixture outside the body with a solution of ricin is capable of rendering the latter innocuous.

Having in mind the production of immunity to this substance, I have experimented on rabbits with dog-serum, but so far without success. On the contrary, I found that animals that had withstood one dose of dog's serum would succumb to a second dose, given after the lapse of some days, or weeks, even when this dose was sub-lethal for a control-animal.

Two rabbits received ½ of 1 per cent. and 1 per cent. of their body-weight respectively of dog's serum, twenty-four hours old, on January 19, 1894. With the exception of hemoglobinuria, indisposition to move, and increased respiration, no ill-effects were noted. The animals still showed hemoglobinuria on the following day. These symptoms disappeared, and apparently the rabbits entirely recovered. On February 12, 1894, each received 1 per cent. of their body-weight of dog's serum intravenously. A control-animal also received 1 per cent. of its body-weight of the same serum. The two animals that had been previously inoculated died in two and twelve hours respectively; the control-animal showed only hemoglobinuria, which disappeared after a day or two.

The pathologic lesions produced in animals by these various poisonous substances have been very imperfectly studied up to the present time. The contributions that have been made to this subject refer almost exclusively to the gross changes in organs and tissues, or consider simply the effect that is produced upon the blood, especially the alterations in coagulability. Hellin, who studied, he says, one hundred organs or parts of organs obtained from animals dead of abrin-poisoning, could discover nothing abnormal, except thrombi composed of red blood-corpuscles. The whole pathologic process in these cases has been considered to depend upon an active gastro-enteritis, thrombosis of the vessels of the stomach and intestine, necrosis and ulceration from digestion. To this is to be added, for those cases in which death occurs rapidly with symptoms of convulsions, thrombosis of the cerebral vessels. Just as little attention has been given to the tissue-changes caused by the inoculation of animals with foreign serum. Heretofore it has sufficed to consider as the cause of death in the immediately fatal cases the coagulation of the blood, especially in the right heart and main pulmonary vessels, or the production of widespread capillary thrombosis. All experimenters have, however, encountered cases in which, as death has been delayed for several days, this explanation was insufficient, as thrombi were not demonstrable. Ponfick has shown that the kidneys suffer injury in secreting the hemoglobin liberated by the breaking up of the red blood-corpuscles, and he attributes many cases of death to the resulting nephritis and blocking of the kidney-tubules with methemoglobin casts.

It will be my especial purpose to point out the insuf-

[1] Journal of Physiology, 1887.

[2] Deutsche med. Wochenschrift, 1891.

ficiency of these views. A study of the pathologic changes in the organs has convinced me that the extent, and not the absence of tissue-alterations, is most remarkable.

At this time there are comparatively few that accept the bacterial origin of disease who will question the mode in which the organisms act, *i. e.*, whether it is the presence of the bacteria as such in the tissues, or the products of their vital activities, that is responsible for the harm that is done. Neither the mechanical influence, nor the effects of depriving the body of a certain quantity of oxygen and albumin, will longer suffice to explain their action. It is true that as living beings the bacteria require certain materials in order to build up their bodies and maintain their functions, and these they secure from the available stores of their surroundings, but it is just as certain that in the performance of their activities they produce excrementitious substances, which are in turn discharged into the host. It is to these substances, of which we have already spoken, that the attention of chemists and pathologists has of late been directed. And the study of their composition and properties has not only brought much light into this field of work, but has opened up new avenues of investigation, at the same time awakening new and unexpected hopes for the future of therapeutics.

It is now some three years since Professor Welch and myself[1] published a short communication on the lesions produced in the tissues by the soluble products of diphtheria-bacilli. This paper, following one describing the histologic lesions in kittens, guinea-pigs, and rabbits caused by the inoculation of the bacilli themselves, confirmed in all essential respects the first paper.

The study of the relation of the bacillus diphtheriæ to the disease diphtheria indicated that the constitutional symptoms of the disease, which, in human beings, are often of the gravest nature, were due to an absorbed poison, and not to the organisms themselves. The separation of the poison from cultures in a dry, but impure state, by Roux and Yersin, and the reproduction through its agency of the constitutional symptoms, including the paralysis, of the disease may be said to have been conclusive. Yet it remained to find in the animals experimented upon lesions similar to or identical with those described by Oertel in human beings.

I shall not here undertake to give an account in detail of these changes. They have since been seen and studied by a number of investigators, and constitute an additional link in the chain of evidence of the causal relation of the bacillus diphtheriæ to diphtheria in human beings. But I wish to state that these lesions are found extensively in the tissues. They are present in the lymphatic glands generally, in the spleen, liver, intestinal canal, kidney, and heart-muscle, and are characterized by a death of cells in the affected parts. Strangely enough, the peculiar changes are not equally distributed throughout the affected organs, as one would naturally infer when it is considered that we have to deal with a soluble substance circulating in the blood; but in the lymph-glands and viscera these lesions tend to occur in well-marked areas or foci.

This, then, has brought us face to face with a new problem in pathologic histology. Heretofore we were wont to separate the focal from the diffuse lesions. The latter class, such as commonly attend infections and intoxications, we have long since learned to know under the term given it by Virchow, of "parenchymatous degeneration," the "cloudy swelling" of the older writers. This is the type of lesion that was believed to result from the action of a soluble poisonous substance, in a certain concentration when the influence is continued for some time. The focal lesions, such as tubercle, a focal abscess, were regarded as the result of the lodgment and increase of the particular injurious agent in the areas affected.

Nor are we required to alter our views of the relation of the focal lesions in diphtheria to the soluble poison by the observation of Frosch,[1] since confirmed by several others, that in human beings a few diphtheria-bacilli are often found in the liver, the spleen, and other organs. The number of organisms is, in the first place, altogether insufficient to explain the lesions; there is, moreover, an entire absence of evidence of relation between the organisms and the tissue-changes, and, finally, there are cases in which no organism can be demonstrated, and, in animals, we now know that they are not necessary to the production of the focal lesions.

But I wish to present still more conclusive evidence of the relation between soluble poisons and focal lesions. For example, certain lesions ought long ago to have led to the suspicion that even soluble substances may act upon one part of the body and not upon another.

Consider, for instance, the action of snake-poison. What could be more impressive than the production of capillary focal extravasations of blood in the serous membranes in consequence of a subcutaneous inoculation of the poison? In this case the action of bacteria or other essentially "living agent" can, by the experiments of Mitchell, Reichert, Formad, and others, be entirely excluded.

I have made a series of experiments with poisons of another kind. From the published accounts of the action of ricin and abrin upon animals, little can be learned concerning the minute pathologic changes induced by these bodies. Manifestly these substances offer an opportunity to study the question of the relation of soluble poisons to focal lesions. In them we have, as I have already shown, substances that in many respects resemble the bacterial poisons; and according to Martin, the action of abrin is suggestive of snake-poison. They thus seemed to constitute ideal substances for study.

The first experiments which I made showed me that the picture of the pathologic changes given by Kobert, Hellin, Stillmark, and Ehrlich was very incomplete. In the main, subsequent work enabled me to confirm their results; but they have overlooked, it seems to me, the most striking and significant changes.

The samples of ricin and abrin which I employed in my experiments were made by Merck. The substances, which are supplied in the form of grayish-white amorphous powders, are insoluble in water, but dissolve readily and completely in a 10 per cent. salt-solution. After solution they can be diluted without change by addition of physiologic salt-solution or distilled water.

One of the impressive results in the use of these bodies

[1] Johns Hopkins Bulletin, 1891.

[1] Zeitschrift f. Hygiene u. Infektionskrankheiten, Band xiii, Heft 1, p. 49.

was the certainty of their action. After one has experimented with bacteria, the virulence of which is open to fluctuation, this constancy of action is a very striking characteristic. In this respect, again, we can see an analogy with snake-poison. Kobert has pointed out that 0.03 mg. per kilogram of ricin is fatal to rabbits and cats, and probably dogs, if injected into the veins, and Ehrlich has shown that guinea-pigs are so susceptible that one gram of the substance would suffice to kill not less than 1,500,000 of these animals.

My experiments have been completed only so far as to enable me to report upon the effects produced upon mice, guinea-pigs, and rabbits. I have had among these animals very acute and chronic cases. The acute cases present such a characteristic clinical and pathologic picture as to be unmistakable.

The lesions about to be described could be produced almost with the certainty of a chemic reaction.

I shall not give the detailed protocols of the cases, but will content myself with a description of the pathologic changes in general, and shall, in the first place, summarize a few typical cases.

The intra-venous inoculation of ricin dissolved in 10 per cent. salt-solution in the proportion of 0.3 mg. to 3 mg. per kilogram of weight kills rabbits in from eighteen to twenty-six hours. In the cases of most rapid death, the axillary, inguinal, bronchial, and cervical lymphatic glands are found slightly swollen and softened. The peritoneal cavity may or may not contain an excess of clear fluid; the mesenteric glands at the attachment of the mesentery are also swollen and edematous. The intestines, especially the small intestine, are distended and pale, their contents being soft, glutinous, and grayish-white in color, and resembling in appearance cholera-stools. The patches of Peyer, in both the small and the large intestine, are elevated, swollen, and pale. They present a reticulated aspect in consequence of the greater swelling of the lymphatic follicles than of the intervening mucous membrane. The heart is filled with blood, the right ventricle being especially distended. The blood is fluid; or soft, dark clots may appear. Neither the kidneys nor the lungs show especial alteration. The spleen is slightly swollen and softened, the liver large, soft, and yellow in color.

The animals that receive a smaller dose and live longer, say from twenty to twenty-six hours, show more pronounced lesions. All the superficial lymphatic glands are greatly swollen and dark in color. The spleen is often much enlarged, tense, and deep purplish-red in color. The kidneys are congested; sometimes the adrenals also. The mesenteric glands are much swollen, edematous and hemorrhagic. The peritoneal cavity often contains bloody fluid, and there are many subserous hemorrhages into the peritoneal layer of the intestines and mesentery. In some cases there are so many hemorrhages into the omentum that the picture presented reminds one of snake-poisoning. The intestines are distended with semi-fluid, glutinous contents, which often show streaks of blood. The mucous membrane of the intestines is congested, and here and there small hemorrhages are observed; the latter correspond at times with dilated bloodvessels in the serosa filled with dark, clotted blood. Peyer's patches present the most striking lesions, and are uniformly swollen and congested. The swelling is apparent at once through the serosa upon opening the peritoneal cavity and examining the intestines, and the glands often reach such a size that they project into the lumen of the intestine for a distance of two millimeters. At times small points of hemorrhage occur in and around the swollen patches, which always present a reticulated surface. In the stomach ulcers are sometimes found. The liver is dark in color, often much congested, and presents to the naked eye foci of yellowish or yellowish-white color, which at times are surrounded by hemorrhagic zones. A few of the inoculated animals were pregnant, and in these there were without exception hemorrhages into the fetal sacs.

The microscopic changes are well marked. In the lymph-glands hemorrhages are commonly present, and the vessels are greatly dilated and packed with red blood-corpuscles. Many of the lymphatic elements are necrotic; cells with fragmented nuclei are common, and this fragmentation is often extensive. Intermingled with the foci of fragmentation are numerous karyokinetic figures. The lymphatic apparatus of the intestines shows in an analogous manner the destructive influence of the poison, but in this situation the cell-death is much more extensive, and the swelling of the follicles is clearly due in part to an increase in number of lymphoid elements. Nuclear figures are found in considerable numbers. In the intestines the destructive process is not limited to the lymphatic elements in the follicles, but those in the villi suffer extensively, and the epithelial elements are as little spared. Fragmentation and necrosis with rapid cell-multiplication by karyokinesis are present here also. The spleen shows changes similar to the lymph-glands, and these are localized in part in the Malpighian bodies.

The liver presents in many respects the most interesting changes, and a variety of forms of cell-death are met with in this organ. In the capillaries of the liver, which are greatly dilated, the endothelial cells are sometimes fragmented and necrotic, and the leukocytes suffer a similar change. But in the liver-cells themselves the process reaches its height. The yellowish and yellow-white areas visible to the naked eye correspond to foci of coagulation-necrosis of liver-cells. The liver-cells in these areas are still preserved in some instances, but they are hyaline in appearance and devoid of nuclei. At times the nuclei can still be made out in the form of fragments. In other foci the cells are much altered in appearance and staining properties, and the nuclei have undergone another form of necrosis. They have not fragmented, but have died as a whole, becoming paler and paler until they finally fail to stain, with apparently a synchronous alteration in the cell-protoplasm. Still other cells have given up most of their protoplasmic material and appear as almost empty vesicles, with here and there a trace of protoplasm. Again, a group of cells will be converted into a reticulated substance suggesting fibrin; and, indeed, these foci of necrotic cells often give a reaction with Weigert's fibrin-stain, while the remainder of the tissue does not retain the dye.

These foci of necrosis are often surrounded by large quantities of nuclear detritus—to such an extent, indeed, as to exclude the possibility of its having been derived altogether from the tissue-nuclei. Some of the detritus must have come from emigrated cells, attracted, as we now know commonly happens, to these necrotic foci,

where they suffer the same fate as the tissue-elements. An interesting feature was noticed in connection with the lymphatics in the interlobular spaces of the liver. They were at times choked with nuclear detritus. Manifestly such an amount of nuclear material could not come from the cells lining the lymphatics, nor from the cells of the lymph. There is only one interpretation possible of this appearance: it represents the nuclear detritus of the tissues and emigrated cells which had been swept by the lymph-vessels into the current. To accomplish this it is probable that an increased lymph-current is necessary.

That in the short space of time—about twenty-four hours—rapid cell-proliferation occurs in the lymph-glands we have adequate evidence, and we also have reason to believe that the same thing occurs in the liver. Around a focus of necrosis, about 1 mm. in diameter, in the periphery of which the capillaries were greatly dilated and literally choked with nuelear fragments, there were evidences of cellular proliferation in the rapid multiplication of the liver-cells, forming at times actual giant-cells.

The studies of Podwyssozki[1] have shown that in rabbits, after injury to the liver, cell-division by karyokinesis has already begun on the second day, and by that time the various stages of nuclear division are present. He also observed on one occasion liver-cells with colossal dividing nuclei, in which no indication of division of the cell-bodies could be made out; from these he believed that giant-cells were formed.

That the liver of rabbits under certain circumstances possesses marked capacity for regeneration has been shown by the experiments of Ponfick, who, after removing large portions of the organ, found that compensatory hypertrophy of the remaining parts took place.

In this description I have had nothing to say of the alterations of the blood described by Kobert. The thrombi of red blood-corpuscles which he found were also met with in my specimens. But they cannot, I think, be regarded as playing an essential part in the production of the lesions.

When we attempt to explain the phenomena that we have just described, great difficulties are at once encountered. There are, as will be readily admitted, several questions of no small interest involved. For example, what determines the localization of the activity of the poisonous agent to such a large extent upon certain structures? Why do the lymphatic elements everywhere suffer so disproportionately? Are there in the body special tissues whose function it is to destroy, render innocuous or eliminate the injurious substances? And as regards the lesions in the intestinal tract, is it not a matter of indifference whether we introduce the poisonous agent into the blood, by the stomach, or subcutaneously?

Moreover how are we to account for the selection (for such it seems to be) of certain groups of cells on which the greatest stress of the poison is exerted? Shall we be obliged to fall back upon an hypothesis with which we are familiar enough in form, but as far as ever from understanding? I refer to the assumption of a difference of resistance of certain cell-groups of an organ, in consequence of which they fall an easy prey to the poisons which other cells can resist. Or, again, do the areas of necrosis, as has also been suggested, represent foci of especial enzyme-activity, points at which the poison increases, with the result finally of causing the death of the animal, and the lesion described?

These are fundamental questions and doubtless not all to be answered at the present time. But we have certain facts in our possession, derived from experiments, which may aid us in the solution of some of these problems.

Koeppe,[1] working in Ludwig's laboratory, and proceeding on the basis that the lymph flowing into a lymph-gland is poorer in cells than the outflowing lymph, supposed that if the lymph-entrance and lymph-exit were both closed an increase in the size of the gland would take place. He accordingly ligated the afferent and efferent lymph-vessels of one of the cervical lymphatic glands of the dog, and examined the gland, comparing it with its fellow of the other side. To his entire amazement, he found that after two weeks the gland operated upon was much smaller than its fellow, and showed upon microscopic examination fewer mitotic figures. The interpretation of this experiment seems clear: the lymph is the normal excitant of the lymph-gland, and upon its presence depends the production of lymph-corpuscles within the gland. This conclusion is made the more probable by the further observations of Koeppe, that the arterial blood supplied to the gland, so far from being an aid, is a hindrance to the multiplication of the lymph-corpuscles.

From his experiments on lymph-formation, Heidenhain believed that he had proved that the separation of lymph from the blood does not depend upon a process of filtration, but is to be regarded as due to a secretory activity of the cells lining the capillaries. According to him a number of substances are capable of so acting on the capillary walls in the dog as to cause an elimination of an increased quantity of lymph, amounting often to several times the usual amount as measured by the outflow from the thoracic duct. Among the most active agents are the enzymes, derived from the salivary, pancreatic, and gastric secretions. Although Heidenhain[2] considered that his experiments proved that the increased lymph-flow is quite independent of the blood-pressure, yet Starling[3] has just shown that in a number of his experiments there was an increased capillary pressure in the liver, whence a large part of the lymph was derived, and it will be recalled that in the liver in our experimental animals the capillaries are much dilated, often compressing the rows of liver-cells.

These facts are, I think, very suggestive. On the one hand we have learned that the lymph is an excitant of the lymphatic glands, and on its presence depends the formation of lymphoid cells, and, on the other hand, it has been demonstrated that certain ferments may act as the cause of an increased lymph-flow. It is pertinent, I think, since the histologic evidence that an increased

[1] Ziegler's Beiträge, vol. i.

[1] His u. Braune's Archiv, 1891.

[2] Pflüger's Archiv, Band xlix. See also Hamburger Zeitschrift für Biologie, Band xxx, p. 143.

[3] Starling: Arris and Gale Lectures on the Physiology of Lymph-formation, Lancet, 1894, 3683 et seq.

flow was actually induced by these enzyme-like bodies is before us, to inquire whether or not the rapid increase in the lymphatic elements can in part be attributed to this cause.

The variations in the circulation of the blood in the organs must be considered as bearing on the production of such focally distributed lesions as are here described. That the circulation is not equal in all parts of an organ at all times is indicated by observations upon living animals, and the capillary circulation especially is subject to wide variation.

I would ask a consideration of the effect this difference may have in bringing about such focal effects as we have encountered in the liver. We have seen that the action of the poisonous agent is exerted in part upon the capillary walls. The necrosis, fragmentation and regeneration of endothelium indicate this. I would also point out that the injury to the capillary wall is nowhere so great as in the areas in which the necrosis is found. This fact suggests the possibility that, in certain capillaries in which the circulation was much diminished in rapidity or was temporarily at a standstill at the time when the irritant acted with the greatest intensity, such damage was done the capillary wall that a freer transudation took place into the tissues than elsewhere, resulting in the destruction of cell-groups; and Cohnheim[1] has shown that the lymph will be more concentrated the greater the permeability of the vessel-wall.

I have already alluded to the fact that in such areas there is an abnormal accumulation of leukocytes. The general blood contains an increased number of these cells, but there are relatively many more in the areas of necrosis.

We now know, thanks to the researches of Stahl,[2] Pfeffer,[3] Leber,[4] Buchner,[5] and others,[6] that certain stimuli of a chemic nature attract and repel these as well as other cells. In undergoing necrosis, certain chemic changes take place in the tissues, through which the leukocytes are attracted to them, but some bacterial products are still more positively chemotactic than are those substances derived from cells. In order that this attraction shall be exerted, Pfeffer discovered for the sperm-threads of ferns that the attracting substance could not be equally diffused throughout the fluid, but must exist in a greater concentration in one part than in others. There is then an immediate movement toward the areas of concentration. It seems plausible at least that the poison which is conceived to be in greater concentration in the areas of necrosis exerts a positively attractive influence upon the leukocytes. To test this point the following experiment was made.

Capillary tubes were filled with a solution of ricin in normal salt-solution of varying strength, 1 to 100,000, 1 to 200,000, 1 to 500,000, 1 to 1,000,000, and introduced beneath the skin of rabbits. Control-tubes of sterilized physiologic salt-solution were also introduced. After twenty hours the ricin-solution of 1 to 100,000 proved to be strongly chemotactic, the open end of the tube being plugged by a thrombus of leukocytes, fibrin, and granular material. The weaker solutions exhibited positive chemotactic properties directly in proportion to the concentration. Only a few leukocytes were found in the tubes containing simple salt-solution.

There remains one other class of ricin-cases, those of chronic character. These are more difficult to obtain, and very small doses must therefore be employed. I give a typical case.

On November 9th, a guinea-pig, weighing 600 grams, received 1.5 c.c. of a 1 to 200,000 solution of ricin, subcutaneously. There was considerable local reaction; a hard node appeared over the site of injection, which, however, gradually disappeared. The animal lost weight for several days, but ten days subsequently to the inoculation had about regained the loss. On December 11th, seeming to have recovered, it was allowed to run about freely, and was often noticed to eat voraciously. Notwithstanding this fact, it grew more and more emaciated until December 29th, when its death occurred. At this time its weight was 270 grams.

At the autopsy the emaciation was extreme. The lymphatic glands were not enlarged; the spleen was small and dark, the liver dark. The intestines contained semi-fluid, mucus-like and turbid contents, and the mucous membrane was much attenuated. Cultures made from the organs were entirely negative.

This picture is strikingly different from that observed in the other class of cases, and presents the features of a profound disturbance of nutrition. The microscopic examination of the tissues showed by the amount of iron-containing pigment in the spleen and liver that great hemolysis had taken place. But of especial interest is the occurrence of atrophic patches in the kidneys.

Up to the present time we have considered the histologic lesions that are produced by the vegetable toxic proteids. I would now ask attention to those caused by toxic agents of animal origin.

Thus far my studies have been confined to the action of the blood-serum of man and dogs upon rabbits. We know from the experience of Landois,[1] Ponfick,[2] Daremberg,[3] Buchner,[4] Carter,[5] and others, that the immediate effect of the injection of serum is the destruc- of the red and colorless blood-corpuscles. The animals, as often happens, may succumb immediately, in consequence of thrombosis of the right side of the heart and pulmonary artery, the respiratory function ceasing before the heart's action. Not uncommonly the animals experience less severe effects, and after a variable period of depression, increased frequency of respiration, weakness and hemoglobinuria, apparently recover.

I have found dog's serum strongly globulicidal for rabbits. This statement is based upon the common occurrence of hemoglobinuria that lasted from one to two days, as well as upon actual counts of the number

[1] Allgemeine Pathologie, 1882.

[2] Stahl: Botanische Zeitung, 1884.

[3] W. Pfeffer: Untersuch. a. d. botan. Institut zu Tübingen, Bd. I and II.

[4] Leber: Fortschritte der Medicin, 1888; Die Enstehung der Entzündung, etc., Leipzig, 1891.

[5] Buchner: Berliner klin. Wochenschrift, 1890.

[6] J. Massart and Bordet: Journal de la Soc. R. des Sciences Médicales et Naturelles de Bruxelles, 1890. Steinhaus: Die Aetiologie der acuten Eiterungen, Leipzig, 1889. O. Hertwig: Ueber die physiologische Grundlage der Tuberculin-wirkung, Jena, 1891.

[1] Landois: Med. Centralblatt, 1874, p. 419.

[2] Ponfick: Berl. klin. Wochenschrift, 1874, No. 28. Ponfick u. Bamberg: Arch. f. path. Anat., Bd. lxii, p. 273.

[3] Daremberg: Soc. de Biologie, 1891, p. 719.

[4] Buchner: Münchener med. Wochenschrift, 1892, p. 120.

[5] Carter: University Med. Magazine, 1893, p. 170.

of red blood-corpuscles. Doses of 1.5 per cent. of the body-weight were usually fatal to rabbits. In these cases death occurred either immediately or after ten or twelve hours. Quantities of one per cent. of the body-weight caused profound disturbances, including hemoglobinuria and albuminuria, and less commonly anuria, and in a few instances immediate death. Some of these animals survived several days or weeks, and some even appeared to recover. They were, however, as we have seen, more susceptible to subsequent inoculations.

When death follows at once upon, or soon after the inoculations, it is usual to find thrombi in the right side of the heart, which may extend into the pulmonary artery and its main branches. The rapid breaking up of the corpuscles liberates the fibrin-ferment, with consecutive coagulation of the blood in the vessels. The experiments of Naunyn[1] have shown that the red corpuscles yield the necessary ferment, and those of Schmidt and others that the white corpuscles, which are likewise destroyed by the foreign serum, are especially rich in this substance.

There are cases, however, in which great destruction of corpuscles has occurred, but in which coagulation has not ensued, and, indeed, under these circumstances the coagulability of the blood is diminished. We owe to the researches of Pekelharing,[2] Wooldridge,[3] Löwit,[4] Schmidt,[5] and others[6] a partial understanding of this difference. It will not be possible for me to enter into the details of this matter here; it will suffice to state that much will depend upon the capacity of the organism to dispose of the liberated fibrin-factors and upon their behavior with regard to the calcium-salts of the plasma.

The cases already alluded to, in which the death of the animal is delayed for a time, are of especial interest, as they show certain well-marked lesions. While the observations that I have made are more complete as regards the action of the serum of the dog upon rabbits, the serum derived from human beings apparently acts in much the same way. Permit me to say that these lesions resemble, but are not identical with, those described in connection with the toxalbumins of diphtheria, ricin, and abrin.

The tissues of animals dead of serum-poisoning which I have so far studied consist of the spleen, liver, kidneys, and lymph-glands. In the acute cases the spleen shows a tolerably rich fragmentation of nuclei situated especially in the Malpighian bodies; the liver contains foci of necrosis of liver-cells, and the renal epithelium is degenerated and many methemoglobin-casts block the kidney-tubules.

Of especial interest is an animal that died on the thirteenth day in which very extensive lesions were found:

A rabbit received on December 25, 1893, 1 per cent. of dog's serum, twenty-four hours old, intra-venously, and was dead in twenty minutes after completion of the inoculation. A second rabbit weighing 1200 grams received ½ of 1 per cent. of serum from the same source. There were no immediate perceptible effects. After the lapse of thirty minutes the expressed urine contained hemoglobin-casts. For some days following the inoculation the animal appeared to be in perfect health, but about the seventh day it began to lose in weight, grew perceptibly weaker from day to day, and died on January 6, 1894.

The autopsy showed great emaciation. The peritoneum contained an excess of fluid; the axillary lymph-glands were enlarged; the intestinal lymphatic apparatus was apparently normal. The liver, which was firm in consistence, was roughened externally and dark in color. The kidneys appeared small; their capsules were not adherent, but their surface was granular. In the spleen, which was enlarged, were a number of white wedge-shaped areas, the bases at the capsule, and quite firm in consistence. Attached to the chordæ tendineæ of the tricuspid valve was a calcified thrombus as large as a split-pea. The urine contained albumin and tube-casts.

The microscopic changes were those of chronic interstitial processes in the liver and kidney. In the latter the tubules were in places atrophied and surrounded by a new growth of connective tissue; in other places the tubules were dilated and the epithelium lining then degenerated; but it was in the liver that the pathologic alterations could best be studied. The chronic changes were well-marked here also, and were such an accurate reproduction of cirrhosis in human beings that a separate description seems superfluous. Areas of newly formed and forming connective tissue, proceeding from the portal spaces and also from the capsule, were irregularly distributed throughout the organ; newly formed bile-ducts were numerous; but what was of especial moment was the association with this of another process, viz., acute degenerative changes in the liver-substance, which were often distinctly the starting-places of the sclerotic process.

In rabbits that died at a somewhat earlier period, after five or six days, I have not infrequently found coagulation-necrosis of liver-cells. To these areas leukocytes are not attracted in such numbers as in cases of diphtheria or poisoning with abrin or ricin; and in keeping with this difference I have found that capillary tubes containing dog's serum, when introduced beneath the skin of rabbits and removed after twenty-six hours, showed very slight positive chemotaxis only.

It is possible in the chronic cases to follow the progress of the pathologic process. The degenerative changes and the new growth of connective tissue can be studied side by side. There is necrosis and disintegration of liver-cells, emigration of leukocytes and growth of connective tissue. The new tissue comes both from the surface-capsule and from the inter-lobular connective tissue, but not exclusively from these. Independent new-formations in the midst of the lobule occur, just as there are independent foci of necrosis in this situation. Here and there, where the connective tissue is advancing, the fast disappearing remains of necrotic cells can be seen; but where the sclerotic tissue is already well developed and new bile-ducts are well formed, this is not always possible. Finally, in the spleen, the white nodules resembling infarcts are masses of fibrous tissue.

The changes found in the organs in cases of serum-

[1] Archiv für exp. Pathologie, Bd. i.

[2] Pekelharing: Festschrift f. Virchow, 1891, Untersuchungen über das Fibrin-ferment, Amsterdam, 1892; Ueber die Gerinnung des Blutes, Deutsche med Wochenschrift, 1892.

[3] Wooldridge: Die Gerinnung des Blutes. Leipzig, 1891.

[4] Löwit: Studien zur Physiologie und Pathologie des Blutes und der Lymph. Jena, 1892.

[5] A. Schmidt: Zur Blutlehre, Leipzig, 1892.

[6] Artur et Pagès, Arch. de physiol. ii, 1890. Lilienfeld, Du Bois-Reymond's Archiv, 1892, pp. 115, 167, and 500.

poisoning are, if I mistake not, of no slight importance. They indicate that it is necessary to enlarge our views of the damage that serum is capable of doing, a damage not limited to the corpuscular elements of the blood, for the tissue-cells are not indifferent to its action.

In the end the differences in the action upon the blood and tissues of the toxic agents discussed are not so great as their correspondences—a fact that emphasizes their chemic similarity. These substances so affect the tissue-elements as to cause degeneration and death, and their effects are followed by reparative processes that do not restore the integrity of the tissues. The relation that Weigert[1] several years ago maintained between parenchymatous degeneration and interstitial tissue-proliferation in the kidney, and which Ackermann[2] urged for the liver in chronic phosphorus-poisoning in rabbits, I have been able to follow in the cases mentioned in both organs, although most satisfactory in the liver.

Moreover, the chronic lesions, such as we have just studied, seem to be open to us for experimental study. Heretofore we have had to content ourselves with the production of degenerative changes, and have been excluded from imitating by experiments on lower animals the chronic proliferative processes in the internal organs of man.

In conclusion, the study of the tissue-changes that I have had the privilege of bringing before you has brought us from the consideration of acute degenerative changes of a focal character due to soluble poisons to the realization of the probability of their playing an important part in the production of chronic interstitial changes in animals, which find in cirrhosis of the liver and chronic nephritis analogies in human beings.

CLINICAL MEMORANDA.

CEREBRAL PALSY OF CHILDHOOD FOLLOWING DIPHTHERIA.[3]

BY CASPAR W. SHARPLES, M.D.,
OF SEATTLE, WASH.

COMPARATIVELY recently a group of cases has been recognized as the cerebral palsies of childhood, having definite relations one to another and separate from ordinary infantile palsy. The condition often makes its appearance as a sequel of some acute infectious disease, such as scarlet fever, measles, etc. Most of the cases offered for study are those of months' or years' duration, and when seen they present as the one characteristic a spastic state of the muscles of the affected side, associated, if of long standing, with a decrease in the size and length of the limbs. Many present various evidences of cerebral disturbance, as epilepsy, idiocy, etc. The occurrence of cases of this class of hemiplegia after diphtheria is rare. Among one hundred and sixty cases of spastic hemiplegia tabulated by Wallenberg only three cases followed diphtheria or croup; nine followed measles; thirteen, scarlet fever; and six, epidemic cerebro-spinal meningitis. Of Osler's one hundred and twenty cases none was reported to be due to diphtheria; and if I recall correctly none of the cases tabulated by Dr. Sarah McNutt, in her paper on "Spastic Hemiplegia," followed diphtheria.

To say just what has taken place in the brain in these cases is difficult, for autopsies in cases of recent date are rare, because most of them survive the immediate dangers of the primary condition, and new processes obliterate to some extent the original state of affairs. Sclerosis, then, is the most common condition found, with porencephalon, simple cysts, and softening as rarer conditions.

A recent German journal contained the report of a case very much like the present one. About six days after the diphtheric membrane had disappeared the boy suddenly became comatose; on emanating from this condition he was found completely paralyzed on his right side, and was also aphasic. After the lapse of five months the aphasia had to a great degree disappeared and motion was returning in the arm and leg, although he still presented the hemiplegic gait. This is the only case of the kind of which I have seen any record.

I venture to report this case on account of the infrequent occurrence of similar ones. I am indebted to Dr. L. R. Dawson for the privilege of seeing the case and reporting it.

J. C., a boy, thirteen years old, had an attack of diphtheria a short time after his father recovered from an attack of erysipelas of the face following a scratch from a fall. Before the membrane had disappeared, and although he was apparently doing nicely, his heart began to be irregular and rapid. About midnight, December 4, 1893, he was suddenly paralyzed upon the entire right side. Coma was not deep or long, for in a half-hour the boy realized what was going on around him. No convulsions accompanied the onset. Preceding the attack, during the evening, the child frequently cried out, making a peculiar sort of noise. This was continued during the day and especially if he was disturbed in any way.

I first saw the patient twenty-four hours after the onset of the trouble. His mental state was improving. The right side of the body was the seat of tremors that shook the entire body. These would last off and on for a half-hour and would recur at irregular intervals during the day. The skin was hypersensitive. Touching the leg would cause the boy to cry out as if in pain. The arm did not present these phenomena to the same extent as did the leg. The tendon-reflexes at the time were absent.

Speech was wanting, although the child appeared to understand what was said to him, and was able to make his displeasure known. His heart was behaving very poorly; its action was tumultuous, irregular, and weak, so that death would not have been a surprise at any time, and it so continued for three or four days, gradually coming down to normal. No heart-murmur was detected. The urinary secretion was scant and passed infrequently. The bowels only moved after the administration of drugs or if injections were used.

This report is made four months after the onset. There has gradually been a return of the power of speech and of motion. Motion began to return in about five weeks, when the boy made an effort to walk with assistance, and now he gets along by himself very nicely, with the ordinary hemiplegic gait. For a time, to obtain any motion in the right hand and arm, he had to use the left

[1] Volkmann's Sammlung klin. Vorträge, 1879, Nos. 162, 163.

[2] Virchow's Archiv, 1889, Bd. 115.

[3] Read at the annual meeting of the State Medical Society of Washington, May 2 and 3, 1894.

to the same purpose, when the right would coördinate; yet the use of the left arm did not always excite motion in the right. Two weeks ago when he attempted to squeeze my hand, he made a very strong left-handed contraction and a scarcely perceptible right-handed one. To-day he could raise his arm a short distance from his body, and could extend the little and ring fingers so that they were nearly straight.

Athetosis has not been present, though at times while moving the left arm the fingers of the right would assume a position approaching athetosis. This now has disappeared.

As is common in ordinary hemiplegia and as is characteristic of hemiplegia in children, the tendon-reflexes have been increased. They are more marked in the leg than in the arm. Ankle-clonus could not be elicited. The skin-reflexes are still exaggerated. Electric examination does not show any reaction of degeneration. In both the arm and the leg the galvanic current causes a contraction of the limb—acting, I would say, through the skin, and producing an exaggerated skin-reflex.

The size of the limb has decreased, as shown by the following measurements: The right calf measures 10.6 inches; the left calf 10.9 inches; the right thigh 13.1 inches; the left thigh 13.5 inches; the right forearm 6.5 inches; the left forearm 7 inches; the right biceps 7 inches; the left biceps 7.5 inches.

The aphasic condition has improved and no doubt will continue to improve until the boy can talk fairly well. At first he could not say a word. After commencing to talk he would use the wrong word. "Yes" was the first thing he could say. After naming an object incorrectly, he would recognize his mistake, but could not correct it, and often could not repeat what he was told. He now occasionally joins a couple of words coherently. To-day he said "Papa—Sharples," meaning that his father had brought him to the office. Occasionally he says something "hurts there."

So far there has been no mental deterioration, unless it be that the boy is more irritable than he was. He adds, multiplies, etc., as well as ever.

For a month the galvanic current has been applied, and within this period he has made more rapid improvement than at any previous time; yet I would not attribute too much to electricity.

There are two other points of interest in the family. His mother had paralysis of the palate, so that deglutition was uncertain and speech poor. The sister, a couple of years older than the boy, who was the last of the family afflicted, and had had her feelings much worked upon by her brother's paralysis, had two hysterical seizures in which right hemiplegia was quite well simulated.

It is a matter of common occurrence to find palsies of different types or locations after an attack of diphtheria. These palsies depend on certain local conditions, the most common being a neuritis involving individual nerves, though separate nerves situated in different parts of the body may be affected at the same time.

The motor nerves show more profound changes than the sensory ones. Yet we are too liable in looking at a case of post-diphtheric palsy to consider it a peripheral neuritis and to look no deeper.

In any lesion of the peripheral portion of a nerve, degenerative changes travel up as well as down, and if they enter the cord they do so by means of the posterior roots. In a few cases of post-diphtheric palsy the degenerative changes have been found in the anterior roots, indicating beyond a doubt that the lesion has destroyed some of the cells of the gray matter of the cord. One observer has found in the substance of the cord colonies of the same germs as exist in the membrane of diphtheria, and the nerve-sheaths have also been found infiltrated with the same germs. In one case in which the latter condition existed, the brain contained a number of infarcts.

These facts have been mentioned to show that if diphtheria can be productive of such conditions in the nerves, and more especially in the cord, it would be only reasonable to attribute a similar causative relation to diphtheria followed by cerebral lesions. Yet it may be justly said that if this were the fact cerebral lesions would be more common after diphtheria than they are. It may be true that diphtheria did not have any more relation to this condition in the case here reported than any other septic or infectious process would have had; and the reason for this would appear the stronger when it is considered that the essentially diphtheric palsies are peripheral and due to an inflammation of the nerves.

As to the question of diagnosis, there is no doubt now, nor was there at any time a reasonable one. The case differed from common infantile palsy in the manner of onset, being sudden and immediately complete, while the other develops gradually and progressively. The time of occurrence, in relation to the attack of diphtheria, was as would be expected for both conditions. The loss of consciousness was complete for only a short time, while if there had been an extensive hemorrhage into the brain-substance, this loss would have lasted longer. It was such as comes on from cerebral embolism. Some observer has stated that these cases of hemiplegia may be caused by colonies of germs plugging a vessel. Aphasia indicated the central origin of the lesion, yet if there had been a neuritis of the inferior laryngeal nerves alone, there would have been aphonia. The subsequent state of ataxic aphasia offsets the possibility of any local condition.

All reflexes were gone at first on the affected side, but have returned. For diagnostic purposes at the time of onset they were of no aid. In diphtheric palsy they only return. In our case they have returned and have also become exaggerated. This change indicates the central origin. The tremor and involuntary movements of the right side indicated that some central irritation was taking place.

In one case in which an autopsy was made soon after the hemiplegia, a very small hemorrhage was found. Porencephalon is attributed to plugging of a cerebral vessel, and as so many cases of cerebral palsy of childhood show porencephalon, the embolic origin of these cases must be quite frequent.

One more point I want to mention, and that is that erysipelas occurred in the house just preceding these cases of diphtheria. The same causes evidently act to produce these two conditions, as they are often found associated in the same houses.

NOTE.—This boy has materially improved in speech and motion, and the size of his limbs has also increased.

A CASE OF ELECTRIC SHOCK OF ONE THOUSAND VOLTS; INSENSIBILITY OF PATIENT TO PAIN; RECOVERY.

BY P. S. DONNELLAN, M.D., L R.C.S.,
OF PHILADELPHIA;
VISITING PHYSICIAN TO ST. MARY'S HOSPITAL.

I AM indebted to the courtesy of my colleague, Dr. W. M. L. Coplin, for the privilege of reporting the following case.

On the 20th of April, 1894, J. R., aged forty-four years, while engaged in repairing broken wires for the Bell Telephone Company, grasped the ends of a wire that had crossed an electric light wire, conveying one thousand volts. He received the full force of the current through his body, and was immediately rendered unconscious. He was thrown violently to the ground, and could not be released until the current was broken by a fellow-lineman, who cut the wires apart with a hatchet.

The man was brought to St. Mary's Hospital at 11 A.M., within half an hour of the accident, and I saw him a few minutes after his admission. He was in profound coma, with pupils widely dilated and irresponsive to light, breathing stertorous, face pale and bathed in perspiration. About ten minutes later he vomited, and then became wildly delirious, so that it required the combined efforts of three men to keep him in bed. He moaned and cried incoherently, and tonic and clonic convulsions of a severe type succeeded each other with great rapidity. At this time we were unable to take his temperature on account of his extreme restlessness, but to the hand it appeared about normal. His respirations now lost their stertorous character, and became more of the Cheyne-Stokes variety, averaging about ten per minute for two hours after his admission. The pulse was 80 per minute, of high tension.

At 11.40 A.M. the man was given morphin, gr. $\frac{1}{4}$, by hypodermatic injection; and as the delirium and convulsions did not abate, the injection was repeated at 12.10, and soon afterward he gradually quieted down. About 1.30 P.M., as his respirations were alarmingly feeble, he was given strychnin, gr. $\frac{1}{30}$, by hypodermatic injection with excellent effect. At 2 P.M. he fell into an apparently normal sleep, from which he awoke four hours later, conscious, but slightly dazed, and feeling, as he expressed it, "tired and sore all over." On my visit to the hospital next morning I found that he had slept well during the night; his temperature was 98.8°, his pulse 72, his respiration 18. He complained of pain from a number of severe burns that he received during his contact with the wire. These burns were distributed irregularly in lines over the back, arms and legs, and evidently were caused by the intensity of the current, as the clothing which covered the affected areas showed no signs of having been scorched.

On questioning the patient as to the nature of the accident, he remembered perfectly all of the incidents of his morning's work up to the time when he grasped the wire that conveyed the shock through his body. After that moment he had not the slightest knowledge of what had occurred, and did not suffer the least pain until he awoke at 6 P. M., as already stated, to find himself in bed in the hospital.

The subsequent history of the case was uneventful. The patient made an excellent recovery.

In view of the employment of electricity by the authorities of certain States for the purpose of putting condemned criminals to death, the facts of the case related are of interest. Dr. J. W. Brown[1] has published the history of an electrocution that took place at the prison at Auburn, N. Y., in which the condemned man received a voltage of 1260 through his body for fifty-six seconds, and, being apparently dead, he was released from the straps. To the horror of those present, he gasped for breath and began to revive. He was placed again in the chair, but the current would not work, so that he was removed to the hospital, and developed a train of symptoms precisely similar to those observed in the case that I have reported. A second contact an hour and fifteen minutes later resulted in death in forty seconds. The case attracted great attention at the time, from the supposed agony of the condemned man, who was regarded by the newspapers as a hero on account of his sufferings. According to the statement of our patient, he was absolutely insensible to pain from the instant he received the shock: even the actual discharge of the current caused him no suffering; and were it not for the burning of his skin, he would not have been aware that he had met with an accident.

While it is to be regretted that the public is greatly exposed to accident from contact with currents of high tension on account of the almost universal employment of electricity as a motive and lighting power in our large cities, it seems to me that, so long as capital punishment has to be enforced as a legal penalty, the electric current, properly applied and of sufficiently high tension, is the most humane agent yet devised for putting condemned criminals to death.

1122 WALNUT STREET.

THERAPEUTIC NOTES.

For Bronchorrhea.—

℞.—Copaibæ . . . . . ʒiij.
Tinct. chloroform. comp. . . ♏xx.
Mucilag. acaciæ . . . . . fʒvij.
Liq. potassæ . . . . . fʒj.
Aquæ cinnamomi . . . ad fʒviij—M.
S.—Two tablespoonfuls three times daily.

Practitioner.

To Control the Vomiting of Chloroform-narcosis WARHOLM (*Hygeia*, 1839; *Memorabilien*, xxxviii, 3, 171) recommends the inhalation of vinegar-vapor, upon the basis of a considerable personal experience. A towel or napkin is wetted with vinegar and held before the nostrils of the patient after the narcosis. The inhalation may be permitted *ad libitum*.

Modified Blaud's Pill.—

℞.—Potassii carbonat. . . . gr. ½.
Potassii sulphat. . . . . gr. ij.
Massæ ferri carbonat. . . . gr. iij.—M.
Ft. pil. no. j.

ENGLAND, *Amer. Journ. Pharm.*, vol. lxvi, No. 7.

[1] Medical Record, New York, 1893, vol. xliv, p. 222.

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SATURDAY, AUGUST 4, 1894.

THE CAUSE OF THE FEVER IN THE INFECTIOUS DISEASES.

ATTENTION has more than once been recently directed to the laboratory of PROFESSOR TIZZONI, of Bologna, through the reports of the careful chemic and physiologic researches that have issued from it. One of the latest and most important of these deals with the origin of the fever present in the infectious diseases. The article is by CENTANNI,[1] and the conclusions at which he arrives cannot, when they have become generally known, fail to excite wide interest and to stimulate further investigation in neighboring fields.

CENTANNI'S results, briefly stated, are these: The febrile phenomena occurring in the course of bacterial infection are the consequence of a general intoxication of the patient with a poison, to which he gives the name *pyrotoxina bacterica*. This substance is formed within the bodies of the bacteria themselves, and is entirely distinct from such bacterial poisons as the ptomaïns, enzymes, and toxalbumins. The pyrogenic substance is present in approximately constant amounts in all bacteria, both pathogenic and non-pathogenic, and, though found in the different bacterial species, appears to have in all the same chemic and physiologic properties.

In the preparation of the pyrotoxin, cultures of bacteria several weeks old were first heated and afterward boiled; the dead bacteria were then filtered out, the filtrate concentrated and treated with alcohol, the resulting precipitate being afterward dissolved in distilled water and freed from albuminates by dialysis. By a repetition of the alcoholic precipitation the substance was finally obtained in a comparatively pure state and dried over sulphuric acid.

The pyrotoxin thus prepared is a grayish-white amorphous powder, soluble in water and in glycerin, but insoluble in strong alcohol, ether, or chloroform. It is not injured at the temperature of boiling water. It is very hygroscopic, rapidly becoming fluid when exposed to the air. By the application of various chemic tests it has been shown not to be an albuminoid substance; it differs from the bacterial proteins described by BUCHNER and the nucleins of GAMALEIA, and cannot be classed with the ptomaïns or enzymes. In fact, it is a product that does not fall in any of the groups in which the chemic substances derived from bacteria are at the present time ordinarily arranged.

When injected into animals (rabbits) the pyrotoxin induces all the typical phenomena of a febrile reaction, just as is seen when bacteria themselves, or simple extracts from them, are thus employed. The height of the temperature is directly proportionate to the quantity of the poison administered. The older the cultures used the more intense is the pyrexia, and the steeper are the ascending and descending limbs of the temperature-curve. Marked emaciation, often leading to fatal marasmus, is a characteristic effect of the injections. Serious disturbances of digestion are produced, diarrhea occurs regularly, and loss of appetite is equally constant. Acceleration of the pulse and respiration is frequently associated with marked dyspnea. There is a very evident general weakness, so that the animal staggers when it attempts to rise. At autopsy the intestine is found filled with fluid feces; the vessels are hyperemic; there are signs of excessive secretion of mucus, and Peyer's patches are markedly swollen. The local phenomena at the site of injection vary; if absorption be speedy there may be only edema and hyperemia; if absorption be delayed, by en-

[1] Centanni, E.: Untersuchungen über das Infektionsfieber. Das Fiebergift der Bakterien. Deutsche med. Wochenschr., 1894, Nos. 7 and 8.

closing the pyrotoxin in sterile glass tubes, suppuration may be set up.

CENTANNI separated the pyrotoxin from a large number of varieties of bacteria, both pathogenic and non-pathogenic, and, as we have said, as far as he was able to determine, the products obtained were in all cases, chemically and physiologically, essentially the same. This observation, he thinks, should not occasion surprise, but is rather what should have been expected, as there is plenty of evidence in the literature to prove that cultures of saprophytic bacteria, when injected in sufficient quantity, are capable of causing toxic phenomena, and even death of the animal; besides, the examples of sapremia in human beings produced by non-pathogenic bacteria are so well known that they need only be mentioned to be immediately recalled. As a matter of fact, the earliest studies of fever of bacterial origin, those of TRAUBE and GSCHEIDLEN, were conducted with the putrefactive bacteria, and the pyrogenin of ZUNTZ and ARONSOHN was separated from cultures of the hay-bacillus.

The weakening of the virulence of pathogenic bacteria does not apparently lessen the amount of pyrotoxin in the bacterial bodies. In spore-bearing cultures the extracts are less active than those made from cultures of the same organisms free from spores. CENTANNI is therefore of the opinion that the pyrogenic substance may be included within the spores, and thus be rendered inactive. The pyrotoxin certainly has its origin in the bodies of the bacteria, and most probably, as he thinks, in the chromatic substance. It is possible, he further suggests, that the extracts from certain bacteria owe their activity in the main to the presence of pyrotoxin, and he puts forward tuberculin as an an example, inasmuch as it has been shown repeatedly that a typical tuberculin-reaction can be evoked in tuberculous animals by the injection of extracts of bacteria of different sorts, even of the non-pathogenic varieties.

Cultures of such organisms as the tetanus-bacillus, the influenza-bacillus, and the diphtheria-bacillus contain, of course, other and more important active principles, but the pyrotoxin is always present along with these. The other substances usually act very quickly and powerfully, and may even lead to a fatal termination before the fever-poison has accumulated in sufficient amount in the organism to make its physiologic action clearly manifest. But when these special powerful poisons are destroyed (by heat in the case of toxalbumins, or by extraction with alcohol in the case of ptomaïns) the cultures, like those of all other bacteria, yield on injection the typical febrile phenomena.

That the results of the investigations just outlined, if confirmed, are significant, not alone as far as the general biology of bacteria is concerned, but also particularly with reference to the practical question of a rational therapy for the fever of infectious diseases, goes without saying. It will be necessary henceforth in pyrexia of bacterial origin to recognize a simple intoxication with a perfectly definite poison worthy of being grouped with the intoxications due to tetanotoxin, to ricin, or to abrin.

Inasmuch as it has been possible in many cases, by means of careful vaccination, to produce in animals immunity to the definite bacterial and other vegetable poisons, so that the serum of the animal rendered immune when injected into another animal is capable of nullifying the poison, or of causing the rapid disappearance of the symptoms even after they have once been set up, CENTANNI hoped that he would be able to prepare an antitoxin for this *pyrotoxina bacterica*, and moreover prophesied that, as the pyrotoxin was the same in all bacteria, when once the antitoxin of the fever-poison of a single bacterium had been found, it would be the antitoxin for all pyrexia of bacterial origin. Since his report was published, a second article (by CENTANNI and BRUSCHETTINI[1]) has appeared, in which some experiments are recorded which permit an *à posteriori* view quite in accord with these *à priori* speculations.

BRUSCHETTINI, while experimenting with the influenza-bacillus, had noticed that animals undergoing vaccination very soon failed to react to strong doses of the vaccine, and that the serum of such an animal would not only prevent infection with the influenza-bacillus, but was also capable of bringing about a rapid and considerable depression of the body-temperature. As CENTANNI'S experiments had proved that the fever-poison of the influenza-bacillus was the same as that of other bacteria, what more likely than that the serum immunizing against this disease should prove just as efficacious in combating the fever called forth by infection with other bacteria. CENTANNI and BRUSCHETTINI therefore set to work to test the question in three ways, studying the effect of antitoxic

[1] Centanni, E., und Bruschettini, A.: Untersuchungen über das Infektionsfieber. Das Antitoxin des Bakterienfiebers. Deutsche med. Wochenschr., 1894, No. 12.

serum (obtained from a sheep rendered immune to influenza) on fevers produced (1) by inoculation of pyrotoxin separated from bacteria, or of sterilized cultures; (2) through injection of living cultures of bacteria that set up local infection; and (3) through injection of some of the bacteria that can cause septicemia in rabbits. Space does not permit of a detailed description of the observations made, although many points of interest are recorded; it must suffice for the present to state that the evidence, as far as the work has gone, goes to support the main point sought to be proved—namely, that the serum of an animal vaccinated against the fever induced by one definite species of bacteria exercises its antitoxic influence also against the infection-fevers caused by the most different varieties of bacteria or their pyrotoxin. The influence of the serum is constant, powerful, and continuous, and the protection lasts for at least some time (in one case for seven days).

All these results are most encouraging, but it must be confessed that the antipyrotoxin has not been isolated in purity, that the experiments have all come from one laboratory, and that they are not as yet very numerous. As the science of bacterial toxicology is much younger than that of bacteriology itself, and as we are only now freeing ourselves from too wide generalizations made in bacteriology, it is, above all things, necessary to guard against hasty conclusions and the acceptance, without mental reservation, of new views until they have been approved and confirmed by a number of workers. Nor is it justifiable, as more than one bitter experience has taught, to transfer the result of animal experiments *ohne weiteres* to the domain of human physiology and pathology. After we have satisfied ourselves of the constancy of the results in animals, numerous trials and observations by competent and trustworthy men in large hospitals must be made before general conclusions are warranted.

EDITORIAL COMMENTS.

The British Medical Association.—Through the fraternal courtesy of the *British Medical Journal* we are in a position to present to-day in an abridged form the Address of the President, the Address on Medicine, and the Address on Surgery, delivered before the sixty-second annual meeting of the British Medical Association just held at Bristol. It is a source of no little gratification to be able to publish simultaneously with our distinguished English cotemporary a partial report of the work of the great medical body of which it is so worthy a representative. We would especially commend to the consideration of educators, surgeons, and the general profession the timely and valuable suggestions offered by Mr. Greig Smith in his charming and interesting Address on Surgery.

A National Bureau of Health.—Having wasted much valuable time, and having kept the country all the while on the ragged edge of uncertainty, it is to be fervently hoped that the present Congress will not adjourn without making a law the bill before it for the creation of a National Bureau of Health. With the threatenings of cholera all over Europe and the actual existence of the disease in many places, and with the further possibility of an invasion of the bubonic plague now playing such havoc in China, the new body might soon be able to demonstrate the justification of its establishment.

Immoral Massage.—The *British Medical Journal* has called attention to a form of immorality which it has discovered is practised in some parts of London under the name of "massage." As a result of this exposure the police authorities have taken the matter in hand, and it is likely that the abuse will thus be repressed. The *Journal* calls attention to the social elements involved in the question of directing massage, and makes a timely criticism of the employment of a masseur in the treatment of women on the one hand and of a masseuse in the treatment of males on the other hand. Massage of the uterus the *Journal* regards with suspicion and dislike and would taboo generally.

Ophthalmia Neonatorum.—The outbreak of an epidemic of ophthalmia neonatorum in the tenement-district of New York City should impress legislators with the urgent necessity of enacting such laws as will tend to prevent, as far as possible, the occurrence of the infection and to check its continuance and extension should any case arise. The cost of the necessary measures would be far less than the pecuniary loss entailed upon the community by the loss of vision and other concomitants following this virulent affection of delicate and important structures.

Quackery in England.—The British Medical Association, through the energetic Chairman of its Parliamentary Bills Committee, Mr. Ernest Hart, is engaged in a laudable attempt to suppress quackery in England, and to this end has undertaken a collective investigation for the purpose of securing data for presentation to Parliament demonstrating the magnitude of the evil.

CORRESPONDENCE.

THE TRICHLORACETIC-ACID TEST FOR THE DETECTION OF SERUM-ALBUMIN IN URINE.

To the Editor of THE MEDICAL NEWS,

SIR: In an article entitled "A Serious Fallacy Attending the Employment of Certain Delicate Tests for the Detection of Serum-albumin in the Urine, especially the Trichloracetic-acid Test," in THE MEDICAL NEWS

of May 5, 1894, p. 477, Dr. D. D. Stewart speaks of trichloracetic acid as an "absolutely uncertain and even dangerous reagent, so likely is it to mislead."

For the introduction of this test into the United States, Dr. D. Meredith Reese, late assistant resident physician at the Johns Hopkins Hospital, is largely responsible. As his work was practically carried on before my eyes, and as I myself have employed the test mentioned, both at the Johns Hopkins Hospital and in private practice, ever since, the number of my individual observations now exceeding five thousand by far, it may not be altogether out of place to say a few words in reference to this matter.

Let us first of all examine a little into the reasons that led Dr. Stewart to look upon trichloracetic acid as such an "uncertain and even dangerous reagent." The statement appears to be based upon an examination of the urine of 105 young men, all of whom, save one, regarded themselves as in good health at the time. The examinations were made in order to ascertain the frequency of reaction to the more delicate tests for albumin of urine from *normal* individuals. On examination, with but three exceptions, all of the 105 specimens gave an "undoubted" response to the trichloracetic-acid solution; of the remaining 102 *normal* individuals, 20 gave an undoubted serum-albumin reaction to nitric acid by the contact-method, so that we may at once throw out these 23 cases, *i. e.*, 21.6 per cent. The conclusion thrusts itself upon the reader's mind rather forcibly, that the "normal" material was rather unfortunately chosen, one person not considering himself in good health, another having a weak heart, being an overtrained athlete; another having a mitral systolic, and still another an aortic diastolic murmur. In but 2 of the 20 cases in which an "undoubted" serum-albumin reaction was obtained with nitric acid, had a microscopic examination of the urine been made, the result, however, not being stated. Dr. Stewart declares that not one of these cases showed evidence of renal disease, a statement that prompts the question whether the examination of a patient's urine for albumin is *altogether* made for the purpose of establishing the existence or non-existence of *renal* disease. Of a physical examination of the remaining 82 cases, Dr. Stewart furthermore makes no mention, but assumes that because in these the nitric-acid test proved negative (I suppose that this examination was made, although no direct statement in this connection is made), "normally urine contains traces of serum-albumin, or more probably that the response to trichloracetic acid was due to the presence of a body of nucleo-albuminous (or mucinous) character of extra-renal origin." In other words, Dr. Stewart appears to regard the boiling and nitric-acid tests as representing the extreme limits of delicacy for the detection of albumin!

Although it might be argued that, as 19 per cent. of "normal" individuals presented traces of albumin in the urine, recognizable by the nitric-acid test, this latter must also be regarded as "uncertain and even dangerous"—a rather precarious position, however, to take—there remains to be considered the fact that the urine of 82 cases among the 105 reacted in a positive manner to the trichloracetic-acid test, and not to the nitric-acid test (that this has been made, I merely infer, as already pointed out), a reaction that Dr. Stewart refers to the presence of a mucinous body. In Reese's work it is pointed out that "that frequent source of error, urinary mucin, or an extra-renal albuminous body, was not regarded in question." On the most careful perusal of Dr. Stewart's work I confess myself unable to find a single statement or experiment in support of the view that he himself (rather cautiously, it is true) expresses—namely, that the trichloracetic-acid reaction obtained by him is referable "more probably" to the presence of a mucinous body, an inference as to the validity of which he "has no doubt."

Rather interesting, not to say naïve, is the manner in which Reese's 14 cases (not only 11, as Stewart has falsely read) are viewed, in which the nitric-acid test was negative, the trichloracetic-acid test positive, and in which granular, hyaline, and epithelial casts were found. To Dr. Stewart these cases are "of especial interest, as they indicate the frequency of non-albuminuric nephritis!" In support of this view, apparently, he cites the words of Dr. Osler, that "word comes over so constantly from the laboratory—'degenerative changes in the kidneys'—in patients whose urine showed no special alterations." I should like to ask Dr. Stewart whether or not he regards the presence of granular, hyaline, and epithelial casts, as found by Reese, as especial alterations of the urine.

When Dr. Stewart then goes on to state that these observations of Reese's "indicate, beyond a doubt, to my mind that the trichloracetic-acid reaction was but a coincidence, obtainable markedly in as many consecutive healthy subjects," in other words, that the reaction obtained was referable to a mucinous substance, he certainly goes a little too far, and has apparently forgotten our modern standpoint in reference to the significance of tube-casts. On page 159, Part II, of Neubauer and Vogel's *Urinary Analysis*, he may find the following: "As to the significance of tube-casts it must be remembered that these, according to our present knowledge, consist of albumin, which coagulates under the influence of the acid reaction of the urine in the renal parenchyma in a peculiar hyaline manner. They merely represent a solidified portion of the albumin held in solution by the urine; their elimination thus essentially indicates the existence of an albuminuria." That these tube-casts, however, consist of a mucinous substance has, as far as I know, never been demonstrated. I can, therefore, see no reason to assume that the trichloracetic-acid reaction in Reese's cases should be referable to the presence of a mucinous body, when the presence of serum-albumin is already demonstrated by the occurrence of tube-casts.

That the association of casts with the reaction obtained by Reese was furthermore not a coincidence, as Dr. Stewart is pleased to regard it, and "obtainable markedly in as many consecutive healthy individuals," is shown by the fact that in 25 cases of Reese's series *no reaction whatsoever was obtained*. It might be argued, that although casts may be present in urine, a positive though faint albumin-reaction may not necessarily be due to serum-albumin, but, as Dr. Stewart would like to have it, to a mucinous body, as cylindruria has been said to occur in the absence of albuminuria. In antagonism to such an argument I should state that I have frequently observed the presence of hyaline tube-casts in urine

when the nitric-acid test and the boiling test with acetic acid were entirely negative, but in which the trichloracetic-acid reaction furnished a positive result; in other words, I can say that with the employment of trichloracetic acid I have never seen a case of cylindruria *sine* albuminuria, a point that I have repeatedly demonstrated to the gentlemen who participated in my course in urinary analysis at the Johns Hopkins Hospital.

A few examples may not be altogether out of place:

CASE I.—Here the urine was light-yellow in color and clear, with a light, flocculent sediment; the reaction was strongly acid, the specific gravity 1020; sugar was absent, the indican moderately increased. There was no reaction on boiling, or with nitric acid; with trichloracetic acid a fine ring was obtained. Microscopically, hyaline and slightly granular casts were found. According to Dr. Stewart, this was a mere coincidence. On physical examination the patient was found to be hemiplegic, the palsy having developed a year before, at the age of fifty-three. There was a high-tension pulse and a ringing aortic second sound. In view of the history of the case and the examination of the patient, it would appear rather dogmatic to regard the positive trichloracetic-acid reaction as a mere coincidence and dependent upon the presence of a mucinous body.

CASE II.—In this the urine was of a dark-amber color, and clear, with a light, flocculent sediment; the reaction was markedly acid, the specific gravity 1030; sugar was absent; the indican moderately increased; there was no reaction on boiling, or on applying the nitric-acid test; with trichloracetic acid, however, a trace of albumin was noted; microscopically, hyaline and granular casts were found. Clinically, the case was one of uremia, with convulsions.

CASE III.—The urine was of a light-amber color, clear and acid, with a light, flocculent sediment and a specific gravity of 1017. A trace of albumin, not demonstrable on boiling or with nitric acid, was noted with trichloracetic acid, together with the presence of hyaline and granular casts. The patient was seventy years old, with well-marked arterio-sclerosis. Death took place a few months later in uremic coma. Shortly before death a large amount of albumin was demonstrated on boiling and with nitric acid.

CASE IV.—The urine was of a light-amber color, clear and acid, with a light, flocculent sediment and a specific gravity of 1021. A trace of albumin was demonstrated with trichloracetic acid, although the reaction on boiling and with nitric acid was negative. There were also hyaline casts. The patient died two weeks later. At the autopsy marked arterio-sclerosis, degenerative changes in the kidneys, and thrombosis of the coronary artery were found.

CASE V.—The urine was light-yellow in color, slightly cloudy, faintly acid, with a specific gravity of 1023. No indican-reaction was obtained. On boiling, after the addition of acetic acid, as well as with nitric acid, no albumin was detected, but with trichloracetic acid a trace was demonstrated. Microscopically, hyaline and slightly granular casts were found. Clinically, the case was one of albuminuria Da Costæ; a few weeks previously albumin was obtained on boiling and with nitric acid to a degree that would have directly excluded the man from life-insurance. The same may be stated of all the cases of albuminuria Da Costæ that I have observed in the course of recovery.

On p. 481 of THE MEDICAL NEWS Dr. Stewart says: "With trichloracetic acid, unless the response be frank and outspoken, . . . the nature of the result must remain in doubt and cannot be utilized to account for the symptoms, if nephritis be suspected, as it is, perhaps, more than likely not due to serum-albumin." From this we may in the first place conclude that the response to the trichloracetic-acid test obtained in his eighty-two positive cases was *not frank and outspoken*—and why then call the reagent uncertain and dangerous. If such be the case, and it could not be otherwise, as Dr. Stewart would then have without doubt agreed that all of his 105 cases were albuminurics, it is rather surprising to me that he speaks in such a positive manner of this reagent as being uncertain and dangerous. On further reading, however, the zone of contact is described as varying from a very narrow ring in the least marked to one of many lines in thickness in the most marked. I must confess that I should always call a ring "many lines in thickness" a frank and outspoken reaction, and in my personal experience at least I am sure that I have never met with such a ring in a *normal* individual.

Now, as far as normal material goes, Dr. Stewart appears to be laboring under the same delusion as Senator and others, namely, that a person must be healthy because he considers himself healthy. In life-insurance work the remarkable health of the applicants is frequently most striking, and only recently have I had in my hands a case of this kind in which all questions as to indigestion, habitual constipation, headaches, etc., were promptly answered in the negative, and a history of unusual health given. In this case albumin was found in large amount, not only demonstrable with the trichloracetic-acid test, but also upon boiling and the addition of nitric acid. The patient later applied to me for treatment, and subsequently furnished the information that his digestion had been miserable for years and years, that he was worn out, felt weak, etc. The cases of Dr. Stewart in which a ring many lines in thickness was observed I should most decidedly regard as cases of true albuminuria, and suggest not only a most careful physical examination, but also an inquiry into digestive derangement, a quantitative estimation of uric acid and oxalic acid in the twenty-four hours' urine, and a careful microscopic examination. To the frequent occurrence of albumin in the urine of young men, particularly associated with an increased elimination of uric acid or oxalic acid, or both, Da Costa has drawn attention in the *American Journal of the Medical Sciences*, 1893, No. 1: a condition that I myself have been able to observe quite frequently.

As far as the "fine ring" is concerned, furthermore, this is merely an optical delusion. Every urine is slightly turbid, and this turbidity will become more marked, and particularly so at the point of contact when brought together with a clear solution, and becoming more marked as the specific gravity of the reagent used approaches that of the urine. With nitric acid this is less marked than in the case of the trichloracetic-acid solution, the specific gravity of the former being greater than that of the latter. In this respect I fully agree with Dr. Stewart when he says that the reaction must be frank and outspoken, but differ

with him in so far that, as I have already stated, I must regard a ring many lines in thickness as a plain and outspoken reaction, such as is not to be found in a normal individual. I should also state that I have applied the trichloracetic-acid test to urine of both normal and pathologic subjects hundreds and hundreds of times with a negative result.

In conclusion, I wish to correct an erroneous statement that Dr. Stewart makes when he says: "Since writing the foregoing I have learned that trichloracetic acid has ceased to be regarded with its former favor in this—the Johns Hopkins—hospital, especially by Professor Kelly, for the reason stated—its impracticable delicacy." The trichloracetic-acid test is used in Dr. Osler's department now, as formerly, whenever in any case the nitric-acid test and that of boiling failed and the case is regarded of sufficient importance to warrant a more careful examination of the urine. In the report of the urinary examination of ninety-one gynecologic cases by Howard A. Kelly, M.D., and Albert A. Ghriskey, M.D. (*Johns Hopkins Hospital Reports*, 1890), the following may be read: "The promptness of the reaction with trichloracetic acid, as well as its delicacy, commends its use." At the present time it is true that the acid is no longer used in Dr. Kelly's department on account of its delicacy, and I freely admit that its delicacy is too great for the surgeon in general, who looks for definite renal changes, *i.e.*, for the existence or non-existence of nephritis. I must, however, emphasize that it is high time that both surgeons and internal clinicians should recognize the fact that the presence of albumin in the urine is not necessarily indicative of nephritis, and is not so in the majority of the cases in which it is found, and that the subject of albuminuria is now undergoing the same process of evolution that we have seen occur in the case of dyspepsia. Our attention and energy should be directed toward a scientific classification of the various forms of albuminuria, and the clinical recognition of the association of albuminuria with definite metabolic disturbances, rather than toward fault-finding with tests as to the practicability and extreme value of which there appears to be no doubt.

Respectfully, CHARLES E. SIMON.

1302 MADISON AV., BALTIMORE, MD.

To the Editor of THE MEDICAL NEWS,

SIR: I beg to thank you for referring to me for brief reply Dr. Simon's rather voluminous protest to the conclusions of my paper on fallacies attending the employment of delicate tests for albumin in the urine. Stripped of quibble and repetition, Dr. Simon's criticism amounts to the following: The material furnishing results was unfortunately chosen; a number of the 105 cases were not "normal" individuals; in those that were and the reaction consisted of a fine ring, the latter was an "optical delusion." Dr. Simon's own experiments with trichloracetic acid have invariably shown that a reaction with this reagent is a reliable proof of a departure from health, indicating disease, renal or otherwise. Incidentally several errors in statement are asserted to occur in my paper.

I distinctly stated in the article criticised, that it was not an inquiry into the frequency of a so-called physiologic or functional albuminuria. It was prepared to form part of a discussion at the meeting of a medical society, and was intended merely as a preliminary introduction to a general study of the subject of albuminuria. It represented a brief inquiry as to the frequency of reaction of urine to certain delicate tests, from a fairly large body of young men who regarded themselves as in ordinary health. The specimens, as stated, were collected for me by Dr. L. Wolff (from his class in urin-analysis in Jefferson College) and are still regarded by him, I am permitted to say, as representing unusually fair material for such experiments. Dr. Wolff, in announcing to the class the object for which the specimens were desired, conscientiously endeavored to fulfil my wish, so far as was possible, to procure the urine of "*normal individuals, those* [in other words] *so far as was known that were without evidence of renal disease.*" Dr. Simon, in disregarding this important limiting clause, as he does whenever he quotes the word *normal*, perverts my very obvious meaning. If he had given a little attention to the literature of the subject of functional *albuminuria major* he would have found that my percentage of gross albuminurics, in nearly all of whom the presence of albumin in the urine was found to be cyclic and probably the result of fatigue, was, though high, not remarkable. He would have found that it is not uncommon to occasionally obtain a marked albumin-reaction to nitric acid (such as would also be "frank and outspoken" with trichloracetic acid) in a subject normal as regards other evidence of nephritis than the presence of albumin.[1] In a second series of thirty-five cases, mentioned in my paper dealing with the reactions of nucleo-albumin, which appeared in THE NEWS, July 14, 1894, p. 29, nearly all of which were furnished by Dr. G. M. Gould from among his acquaintances, the reaction with trichloracetic acid was also positive. These were, as detailed, morning specimens from young adults in apparently robust health. In none of the total 140 was there the slightest cause evident for deception on the part of the donors as to their physical condition, as might be the case in life-insurance or civil (compulsory) examination. I was previously unacquainted with any of those contributing save six. The two with cardiac murmurs, which were discovered as the result of subsequent examination, were, like ourselves, previously unaware of the existence of a heart-lesion. The fact being very apparent, after a large number of these examinations had been made, that probably all normal urines reacted to trichloracetic acid, it was not deemed necessary, in view of the amount of work that would be entailed, without a number of assistants, to make exhaustive physical examination of all those concontributing, or undertake microscopic examinations of the urine other than the specimens reacting to the less delicate tests. Microscopic examination was made in most of the cases of major albuminuria as well as frequent chemical examination of specimens of urine furnished by these on other occasions. The paper, prepared as it was to form a part of a discussion, was written before these details could receive adequate attention. As to the nineteen cases that I stated showed no

[1] My meaning of the words "frank and outspoken" as applied to the extent of the trichloracetic-acid ring, as indicated by the context (THE NEWS, May 5, 1894, p. 481, 2d col., 3d par.), is so evident that it is needless to notice the portions of Dr. Simon's criticism referring to them.

evidence of renal disease, and concerning which Dr. Simon makes an inquiry, he will find that the context of the portion of my paper referring to this point shows that it is to *physical examination* that I refer.

In the application of the tests as detailed I was careful that another beside myself should simultaneously view the results obtained, in order that all question of error should be eliminated. In the series of 105 examinations I had the kind coöperation of Dr. Henry Leffmann, a chemist of whose repute it is unnecessary to speak. In the second series, mentioned in the later paper, in which trichloracetic acid was the only delicate test employed, the results were studied with me by Dr. L. Wolff, who, as is well known, has for years been demonstrator of chemistry and urinology in Jefferson Medical College. So that, in view of the agreement of these gentlemen with me as to the nature of the results as criticised, an attempt on Dr. Simon's part to explain as an "optical delusion" the more delicate reactions obtained, which in his work he is unable to note, save in selected cases, is simply puerile, and not worth discussion. It may, however, be stated that the influence of shading, inclination of tube, and especially the effects of heat, rendered all chance of illusion impossible, even were his curious statement as to the relative specific gravity of nitric acid and trichloracetic acid accurate. This statement, however, is both inaccurate and misleading. The solution of trichloracetic acid as employed by me was a thoroughly saturated one, as Dr. Simon should have seen from reading my paper, for I lay stress on this. This same solution is always presumed to be used in testing for albumin, and it was stated to have been employed by Dr. Reese in his experiments. Now, while the specific gravity of nitric acid is 1.41, that of a saturated solution of trichloracetic acid is considerably greater than this. A solution recently made, and now on my shelves, has a gravity of 1.56. This, from the manner of its preparation, is regarded as of somewhat less density than that employed in the experiments. In my paper especial stress was laid upon variation in result due to carelessness in the preparation of a concentrated solution. It is probably to some such fault in technique as this that Dr. Simon's lack of result is due, and if he is using a dilute solution he may have encountered optical illusions of the nature of which he writes. If, however, an optical "delusion" could be thus produced, it would become evident, if not with nitric acid, at least with picric acid solution, with Millard's test, and other reagents whose specific gravity more nearly than trichloracetic acid approaches that of urine; but this source of error, I am confident, can be excluded. But merely for the sake of argument, granting that those trained in urinalysis might be deceived through an optical error, then this would be the very best argument against the practical utility of the trichloracetic-acid test, for Dr. Simon apparently reserves for himself alone the power which he denies others also trained in chemical manipulation, of distinguishing between an "optical delusion" and an actual, fine ring, significant of a trace of albumin. For, on turning to the report of the five cases in his letter, it is evident that this same fine ring which I have shown may be encountered in the urine of all in health, was present in each. It is stated that in none of the five did a reaction occur with heat or with nitric acid, but that in the first "with trichloracetic acid a fine ring was obtained," and in the others also, a "trace of albumin" was so noted!

As to "our modern standpoint in reference to the significance of tube-casts," that their existence depends upon the presence of albumin, I would refer Dr. Simon to literature more modern than that which he quotes, which assigns a totally different origin for renal cylinders. This view, which I believe is that now generally accepted in preference to the more antiquated and less probable one cited, Dr. Simon will find, with certain references, in the latter part of a paper by myself in THE NEWS of April 14, 1894, p. 393. It is there stated why I hold that serum-albumin (or globulin) may be absent and nucleo-albumin present in certain cases in which casts are detected in the urine.

Several of Dr. Simon's statements, however foreign they are to the point at issue as to the utility of trichloracetic acid as a clinical test for albumin, and quibbling as they do with the facts, demand special notice, as, uncorrected, they must inevitably lead to a false impression in the minds of readers not familiar with my work. With a careless disregard for accuracy, in unison with the general tenor of his letter, he states that I have falsely read Dr. Reese's figures. I have but to refer to that portion of my paper in which this so-called false reading appears to show how absolutely incorrect such a statement is. After remarking that many cases had been encountered, the urine of which responded only to trichloracetic acid, I further remark that "in a number of these cases (11) granular, epithelial, and hyaline casts were found." Dr. Reese's report distinctly reads: "In 11 of these cases granular, epithelial, and hyaline casts were found."[1]

Again, the statement that I appear "*to regard the boiling and nitric-acid tests as representing the extreme limit of delicacy for the detection of albumin!*" is totally without warrant. My meaning clearly is, as any one unbiased reading my paper will acknowledge, that these tests represent, from our present knowledge, the limit of *practicable* delicacy; and there is no question that the most conservative of internal clinicians are rapidly coming to this conclusion. Among a large number holding the view that Dr. Simon criticises, I need only mention Tyson, of Philadelphia, and Saundby, of Bristol;[2] and Shattuck,[3] of Harvard, who thinks similarly, in a recent paper on the subject of albuminuria quotes Prof. E. S. Wood, of the same school, as also of this view. This opinion was also strongly maintained in the recent discussion of my paper on "Nucleo-albumin" before the College of Physicians of Philadelphia. Such men as Prof. J. M. Da Costa and Prof. J. P. Crozer Griffith questioned the practical utility of the more delicate tests. Prof. Da Costa remarked: "I am more and more coming to the conclusion that delicate tests for albumin are of little use to the clinician. I believe the saying of Grainger Stewart to be correct, that 'if heat and nitric acid properly applied show no trace of albumin, albumin may for practical purposes be discarded.'" That this view is

[1] Johns Hopkins Bulletin, February, 1890, p. 33.

[2] See my paper on the trichloracetic-acid test in THE NEWS, May 5, 1894, p. 477.

[3] Boston Medical and Surgical Journal, June 21, 1894, p. 613.

prevailing among the most enlightened of life-insurance examiners is evident from the fact that at a recent meeting of the Life Assurance Medical Officers' Association, of London, it was held that "urine which did not show a trace of albumin with the boiling and cold nitric-acid tests properly applied might be considered free."[1]

As to the erroneous statement that I am alleged to make concerning the waning favor in which trichloracetic acid is regarded in the Johns Hopkins Hospital, especially by Dr. Kelly, I fancy it is plain enough to any one reading the curiously worded correction of Dr. Simon, that he unconsciously acknowledges the correctness of my assertion. I might here state that as my informant in the matter was Dr. Ghriskey, I had no doubt as to the accuracy of the statement as quoted.

Finally, to conclude, the essence of the whole question is whether or not the trichloracetic-acid test is or is not of practicable clinical delicacy. My own view, further elaborated in the paper on nucleo-albumin (THE NEWS of July 14, 1894), and based on good evidence, is very decided as to its inutility. I show that, with *careful* technique, the indications point to an albumin-reaction being obtained with any specimen of all urines from the healthy. The questions there considered, as to the nature of the albuminous body reacting, whether serum-albumin or nucleo-albumin, is without practical bearing on the point at issue. That an albumin-response may be unquestionably obtained in all urines indistinguishable from that of serum-albumin, my results in a series of now over 150 consecutive cases so strongly show that I am forced to the conclusion that Dr. Simon's negative results in his large number of cases must simply be due to lack of proper technique in the application of the test, or to failure of observation; there is no other explanation tenable, and direct evidence of the former is at hand in his statement as to the density of the solution of trichloracetic acid used by him.

It is, perhaps, unnecessary to state that I shall be glad to practically demonstrate the correctness of my conclusions to any one sufficiently interested who will furnish specimens of urine from those not renal suspects.

Respectfully, D. D. STEWART.

2620 N. FIFTH STREET, PHILADELPHIA.

SOCIETY PROCEEDINGS.

BRITISH MEDICAL ASSOCIATION.[2]

Sixty-second Annual Meeting held at Bristol, July 31, August 1, 2, and 3, 1894.

FIRST DAY—JULY 31ST.

DR. EDWARD LONG FOX, of Bristol, delivered the President's Address, which was entitled "On the Medical Man and the State." After a word of thanks, and after extending a hearty welcome, reference was made to the last meeting of the Association held at Bristol, which was the thirty-first, and had taken place thirty-one years before. Then the work of the meeting had not yet been divided into sections, and no one dreamed of the pecuniary condition of the Association ever being what it is today, or that branches would be planted, as they are, in most of the British Colonies and dependencies.

As a body the medical profession is above party. Its highest aspirations tend to the formation of a pure commonwealth. The poor, the sick, the criminal are its daily study, primarily for the relief of the individual, but with nobler and farther-reaching aims, namely, that poverty may be mitigated by more healthy surroundings; that sickness may be diminished by the education of the nation in the wiser laws of health, by increased temperance, and by knowledge from an early age of the common facts of physiology; and that the criminal class in the future may occupy narrower limits, because no longer the victims of a debased heredity. Poverty, disease, and crime—these are the objects of its investigations as a body, these are the foul blots in the State for which it seeks amelioration.

What numbers of intellectual people, whose work should be so high in poetry, in art, in political or professional life, in commercial undertakings, and even in manual labor, are unfitted for giving their best to the State by an unhealthy environment, by ignorance how to use and how to husband their brain-power, or by yielding to this or that self-indulgence, the very yielding a neurosis! It is but a truism to say that a model State needs the best intellect of each and all her children. Medical men have to work against hereditary influences, induced by the ignorance of many preceding generations—the "good old times," as they are so fondly and so falsely called. But the work is being done. From the highest to the lowest in the State each individual must be brought to recognize that his power of doing good, of duly filling his appointed place in the commonwealth, of carrying out the highest form of altruism, depends in wide measure on his ruling his life in accordance with physiologic laws, for a knowledge of which the world is mainly indebted to members of the medical profession.

All science is cosmopolitan, and medical science, perhaps, especially so. This or that point may have been brought into prominent notice in England, on the Continent, in America, or elsewhere. But the profession in every State is quick to recognize everything that bears upon the subject it has at heart, the well-being of the human race.

Step by step the need of medical guidance is permeating more or less every branch of the public service. *Experientia docet.* What thousands of lives have been saved by the careful observation of the sources of disease by medical men in various parts of the world! by none more ably than by the medical officers of the naval and military services. In their observations upon cholera, yellow fever, and the various forms of malaria, for instance, especially such as in some of their symptoms simulate yellow fever, some of the best work has been done by the medical officers of the army and navy.

The chief need of an ideal State, apart from the legislative and executive departments, is, that the people should be healthy, strong, temperate, and wise. Whatever the form of government, whatever the strife of parties, the nation made up of indi-

[1] See British Medical Journal, June 16, 1894, p. 1324.

[2] Prepared from advance-sheets kindly furnished by the British Medical Journal.

viduals is the only ruler. The medical profession has to deal first with individuals, and then with conglomerate bodies of men. Granted a strong development, founded partly at least on obedience to the facts of heredity and on good sanitary laws, the race will and must advance in all physical and mental conditions. So far from being considered, as in Plato's time, as either gainers of money or tenders only of the sick, it is the proud boast of the profession that much of the medical thought of the day, and for many years past, has been devoted to the prevention of disease.

Speaking of Jenner, it was said that he not only created a sure method for the prevention of the most terrible scourge England has ever known, but unwittingly laid the foundation of all microbic pathology. His reward was that each year he saved from death in England alone thousands of lives; and perhaps three times as many owed to him their immunity from the disfigurement and the local diseases consequent on smallpox. It was considered monstrous that in less than one hundred years from the birth of vaccination, the great work of this benefactor to the State should be rendered partially ineffectual by the crazy cry of the liberty of the subject. Should the men be left untouched and unhindered, who, from faddish fears of the evils of vaccination—evils that might be entirely avoided by the use of calf-lymph—are endangering thousands of their fellow-citizens, and doing their utmost to interfere with the only reward to which Jenner looked forward, the well-being of the human race?

It is in the realm of investigation that the medical profession has given some of the best service to the State. Enormous advantages have been conferred upon the State by the light thrown by many investigators on the subject of bacteriology. Already much is known about abscess, enteric fever, diphtheria, cholera, pneumonia, tuberculosis, tetanus, and glanders. Already M. Pasteur's investigations have brought the death-rate from rabies to less than 1 per cent. Already, through the efforts of the same great experimentalist, millions of sheep are being inoculated against anthrax in various parts of the world. Already antiseptic surgery, the splendid result of the work of Sir Joseph Lister, may claim to have made possible hundreds of operations, hitherto too dangerous to attempt, and to have saved thousands of lives. The whole course of medical treatment is being revolutionized by these studies. The coming generation of doctors will have their time taken up, even more largely than in past years, in rendering persons immune to the attacks of disease. It is known now that abscesses caused by staphylococci have a tendency to remain localized, whilst those from streptococci are often followed by metastatic abscesses, as in erysipelas, puerperal fever, and ulcerative endocarditis.

It is now known that the tubercle-bacillus is found in chronic bone-disease, and that if present alone the disease is a chronic one, whilst if the streptococcus pyogenes is present also the disease is more quickly fatal; that the suppurations accompanying tuberculosis are due, partly to the tubercle-bacillus itself, or, rather to the poisons resulting from the action of that bacillus, but partly also to other microörganisms; that the bacillus diphtheriæ is found chiefly on the surface of the false membrane, and that the fatality of the disease depends on the poison secreted by the bacillus, whilst the presence of streptococci renders the disease more grave, the increased virulence being due to the presence of both these organisms together. Acute pneumonia is caused by the pneumococcus of Talamon-Fraenkel, although often in association with the streptococcus pyogenes. This pneumococcus, too, may produce abscesses in patients free from pneumonia, as in purulent pleurisy, ulcerative endocarditis, and suppuration of the nasal fossæ. The fact that this microbe is present in the saliva of healthy people proves that these diseases have also a non-microbic element. Some condition of the sympathetic influencing the caliber of the bloodvessels or some morbid condition of the vagus or of the accelerator nerves, or some inherited vulnerability, with all its possibilities, must probably be a precedent factor. The typhoid-bacillus is often accompanied by other microörganisms, especially the streptococcus pyogenes or the staphylococcus aureus and albus. The study, too, of tetanus might, if time permitted, open up a further story of the mode of destruction of these microörganisms, as the leukocytes refuse to take into their interior the tetanic bacillus when other microörganisms are present in the wound at the same time.

Is it not remarkable that in a practical country like Great Britain the existence of such beneficial institutions as Research Laboratories is left to the liberality of private individuals? Is it not remarkable that the State has nothing to do with them, except by utilizing the advances in preventive medicine, engendered by the labors of those that are connected with them.

Perhaps next in importance to the study of bacteriology is the good work done by medical men, and in part acted on by Parliament, on the subject of noxious trades. Here especially does the State owe much to members of the medical profession.

There is now no portion of the human frame in which disease is not being traced to its source by medical philosophers with a view to its prevention or its cure. In no department has better work been done than in the investigations of the nervous system. In no department has the result of such investigations been of more permanent utility to the well-being of the State.

What is still partially needed for the brain itself has been in large measure accomplished for the medulla oblongata. How many lives have been preserved to the State by the more accurate knowledge of this small portion of the nervous system. Forming a connection between the brain and spinal cord, in some respects belonging to the spinal, in others to the cerebral system, how many centers are represented here.

Sympathetic reference was made to the late Prof. Charcot.

Good work has been done in the medical investigations of akromegaly and myxedema. The peculiar

symptoms classed under the latter denomination are strikingly improved by the injection of the organic liquid extract from the thyroid gland. This is only one instance of the benefit conferred by the use of these organic liquid extracts from the glands and other organs. The use of cerebrin in neurasthenia, tabes, and even in some cases of epilepsy, of thymus fluid in pseudo-hypertrophic paralysis, of a liquid extracted from the medulla of the bones in the treatment of anemia, debility, and lymph-adenoma, opens up a new line of thought both in physiology and therapeutics. The value and importance of such investigations is still *sub judice;* but when, as in myxedema, some morbid condition of the system depends upon the absence or disease of a certain organ, it was not unreasonable to hope that the exhibition of this organ, or of healthy preparations from it, might be beneficial. And this mode of experimental therapeutics will lead to a better classification of disease and to the power of generalization of many morbid phenomena that hitherto have been absolutely unrelated.

This new mode of treating myxedema leads up also to the question of feeble-mindedness in children, cretinism, and especially sporadic cretinism, which is only myxedema in childhood.

The subject touches biologists on questions of heredity, surgeons with reference to the relief of synostosis, and physicians, legislators, and criminal lawyers in its various phases. It is being learned that, except in the case of the microcephalous, cranial developments do not help much in these researches—not even pathologic appearances. The power of attention, and the consequent results of education, are almost the only trustworthy data for differentiation. But this benefit to the State, due mainly to members of the medical profession, obtains not only in raising some of these afflicted ones to a dim apprehension of the abstract, but many more to a condition in which they are partially, at least, able to earn their own living, and be no longer wholly a burden to the community.

It is a mere truism, more or less generally recognized, that for hard work, for self-abnegation, for devotion to the good of others, the medical profession, from student-life onward, is a type for the imitation of the nation at large. Plato spoke of medical men with some disdain as "gainers of money," but that sneer can never be applied to the medical Poor-law officers. Amid the constant pressure of hard work, amid difficulties of all sorts and kinds, with continual disturbance of rest, and with demands on their mental resources more incessant than is usually experienced among the rich, the Poor-law medical officer, either at the workhouse or in district-work, knows no repose, and with a salary so inadequate that the State ought never to sanction it, becomes the hearty and untiring friend of the poor, a pillar of the State not only by the results of his devotion to his duties, but by the splendid example of his life.

But professional influence permeates the nation in many directions. It is the enemy of excess of all kinds. The medical experience of the day has set itself against excess. And not only as to food. A vast number of the profession may not be total abstainers from alcohol, but the majority are examples and teachers of temperance.

They were medical men who made experimental observations that placed this question on a basis of truth and common sense. How important is it for the nation to know that alcohol is, with certain exceptions, unfitted for childhood; that any excess in muscular work, as in the forced march of an army, is rendered far more difficult by its use; that it not only fails in giving power in the work of the muscles and the heart, but acts distinctly as a depressant; that it never enhances the temperature of the body, and that in its pure state it is in no sense food.

It is to medical influence that the sensible care of children, the due relation of muscular and of mental work in schools, the methods for regulating the health of body and mind amid the railway pace of modern life, the prolongation of existence to a ripe old age, are almost wholly due. What assistance, too, does it give so often to the law, though doubtless in this relation it would be better that in controversial cases the medical witnesses on each side should meet in consultation.

SECOND DAY—AUGUST 1ST.

The Address in Medicine was delivered by SIR T. GRAINGER STEWART, of Edinburgh. He took up for consideration the nature and treatment of influenza.

He cited evidence of an epidemic occurring on the Continent of Europe in 1387 and of another in Scotland in 1562. Particular reference was made to the complications and sequelæ of the disease.

The alimentary system was affected in a great variety of ways. Apart from the disturbance attending the acute attack or primary disease many patients suffered for weeks or months afterward from various digestive troubles. In such cases there was no doubt that the gastric symptoms were due to influenza, but it was not easy to say whether the gastric mucous membrane was the structure primarily affected, or whether the nerves supplying the stomach were at fault.

The hemopoietic system exhibited innumerable changes. Ordinary anemia was commonly observed, and forms so severe as to warrant their being called pernicious now and then occurred. But among the most important of the blood-changes noticed was purpura hæmorrhagica.

It is difficult to say how these blood-changes are brought about, but it must be kept in view that at least one of the structures standing in important relation to the blood is affected, namely, the spleen; that it is often enlarged in influenza as it is in so many fevers; and it is not unreasonable to suppose that the bone-marrow and other structures may be similarly involved, and that the blood-changes may be due to these.

But, apart from structural alterations of the blood, chemic changes have been frequently observed to result from influenza. Perhaps the most typical is the occurrence of gout during convalescence from an attack.

Diabetes mellitus has been found to stand related to the influenzal process in two ways—for those who have been suffering from diabetes and have taken influenza showed a proclivity to diabetic coma, and, in a considerable number of cases, the diabetic process itself took origin just after influenza.

It is possible that changes in the central nervous system may afford the explanation of the occurrence of diabetes in the sequence of influenza, or it may be that organs such as the liver or the pancreas, which stand related to the transformation of sugar in the economy, may be directly affected by the morbid process.

The circulatory system exhibited some of the most interesting post-influenzal phenomena and of considerable variety. In some instances the heart's action was unduly slow, in others excessively rapid; in the first instance as a result of a diminution of the action of the cardiac motor nerves; in the second of a diminution of inhibition. In some cases the heart was rapid and irregular, and there existed marked dropsy as a result of increased backward pressure from the failure of the heart's action. In some of these cases it is probable that degenerative changes occurred in the muscular fiber of the organ. In other cases a fatal result occurred from sudden failure of the heart's action, sometimes with, and sometimes without, fatty degeneration of the muscular fiber. Pericarditis was frequent, endocarditis occasional, and perhaps myocarditis also.

The respiratory system suffered changes more frequently in connection with influenza than did any other organs of the body. In some cases bronchitis persisted for a longer or shorter time. In some of these, without doubt, that inflammation was of a specific influenzal character, the bacilli being demonstrable in the sputum all the time. In others it was, perhaps, of a simple non-specific kind. The influenzal process has been observed in relation with bronchitic asthma. The explanation is to be found partly in the local effects of the influenzal process, and partly in the disturbance of the nerves supplying the bronchial tubes, which stand so definitely related to asthma.

Pneumonia was by far the most formidable sequel of influenza, and displayed marked differences of type from the normal course of the disease. Moreover, its fatality appeared to vary in the recent epidemics. Every variety of pneumonia presented itself, but the catarrhal was most frequent, and that of an acute and peculiar type.

The croupous form was also frequent, and pleurisy and empyema accompanied it in a considerable number of instances. In explanation of these complications it may be assumed that the catarrhal pneumonias were due to extension of inflammation from the bronchi to the ultimate air-cells. In the cases of croupous pneumonia the organisms of Friedländer and Fraenkel were abundant enough, and streptococci were found in the empyema cases. There was no reason to suppose that these organisms were more abundant or more active during the influenza-epidemic. The difference lay in the greater susceptibility to the action of the organisms induced by the influenzal process.

The relationships between influenza and pulmonary tuberculosis were equally striking and varied. In not a few instances pulmonary tuberculosis originated in an attack of influenza, and frequently tuberculous patients, whose condition had been quiescent or scarcely advancing, suddenly developed pronounced symptoms, and went on rapidly to a fatal result. The relationship between the two processes seems to depend on the fact that influenza so affects the system as to render it more susceptible to the action of the tubercle-bacillus.

Among the morbid conditions of the integumentary system which attended upon the process may be mentioned the critical efflorescence so often observed at the height of the disease, and the desquamation which speedily followed on that inflammatory action. There was also a tendency to chilliness of the skin, and to copious and exhausting sweating, which often persisted for months after the acute symptoms had passed away.

The urinary system was affected in many ways; sometimes there was a mere passing albuminuria, sometimes a formidable hematuria or serious inflammation of the kidneys, and in some epidemics, as in one of those recently described in Egypt, such changes were frequent, and in a considerable number of instances proved fatal by uremia. Some patients exhibited a susceptibility to vesical inflammation. The reproductive system also showed manifest changes in both sexes—the functions became greatly impaired.

But the nervous system suffered most frequently. In every case of influenza during the acute stage disturbance of that system was pronounced, and nervous sequelæ were extremely common, serious, and persistent.

Eye-changes were numerous, inflammation and ulceration of the cornea, conjunctivitis, iritis, glaucoma, asthenopia, optic neuritis, optic atrophy, paralysis of accommodation, dyschromatopsia, blepharospasm, and many more. Diseases of the ears were common, especially otitis. Changes in the sense of smell and taste were observed; sometimes in the way of diminution, sometimes in the way of perversion, and sometimes in the way of exaggeration of function.

The locomotory system also sometimes showed important changes in respect of bones, joints, and muscles.

This list of complications includes morbid processes which arise in a great variety of ways. An etiologic classification of morbid processes may perhaps serve to render this more distinct.

1. *Diseases which owe their Origin to the Invasion of Foreign Organisms, particularly Microörganisms.* Among the maladies which follow influenza there are undoubtedly several belonging to this group, as, for example, tuberculosis and pneumonia.

2. *Diseases due to Faulty Chemic Action within the Body* either in respect of (1) the introduction of toxic substances from without; (2) faulty gastro-intestinal digestion; (3) faulty chemic transformation of the blood and other elements of the body; or, (4) faulty elimination of waste products. This group is well represented among the after-maladies

of influenza, the gastro-intestinal cases affording illustrations of faulty digestion; the anemias, purpura, diabetes, and many cases of gout affording examples of faulty metabolism, while in some instances gout and other maladies may be induced by faulty elimination.

3. *Diseases dependent upon Faulty Mechanical Conditions.* Illustrations of this group may be found in the swellings of the limbs and other changes following upon thrombosis of veins, and in the dropsies and other results of backward pressure following upon dilatation of the heart.

4. *Diseases dependent upon Faulty Innervation.* Of this group there are abundant examples, as in some of the cardiac and gastro-intestinal disorders, in the feverish attacks, and the profuse perspirations.

5. *Diseases dependent upon Morbid Nutrition of the Tissues, either in the way of Inflammation, New formation, or Degeneration.* Influenza has shown numerous illustrations of the inflammations, as, for example, in the cases of meningitis, pericarditis, pleurisy, neuritis, dermatitis, while the degenerations are illustrated by the fatty changes in the cardiac muscle.

While knowledge of the clinical features of influenza was increased, still greater advances have been made in regard to the essential nature of the influenzal process. The essential cause of this process has been found to be a bacillus presenting distinctive characters in respect of appearance, staining and cultures, and present in the sputum in enormous quantities.

Even to the naked eye influenza-sputum is characteristic enough. It is of a yellow-greenish color, viscid and tough, generally brought up in lumps or balls, and presenting a nummular appearance in the dish. It varies in quantity from a very small amount up to several c.c. in twenty-four hours. In almost every case it is derived from the nose and pharynx, but in those of any severity largely from the bronchial tubes, down to their utmost ramifications, and from the air-cells of the lungs.

The bacilli are, as a rule, present in enormous numbers in the mucus of the respiratory tract. They are to be found also in the mucous membrane, and to some extent in the neighboring tissues. They are met with in the inflamed patches of the lung, along with the ordinary microörganisms of pneumonic processes. They are occasionally found, but in comparatively small numbers, in the blood, and when there they appear to be dead or dying, being no longer capable of cultivation. They may block bloodvessels in patches of inflamed lung, and they have occasionally been found in different parts of the body, as, for example, in the kidney and the liver.

It seems probable that the constitutional symptoms of influenza result indirectly rather than directly, and for several reasons: 1. The bacteria are not found living, active, numerous in the blood and throughout the tissues of the body generally, and therefore cannot be supposed to be operating so widely. 2. The character of the symptoms corresponds to that of those due to such poisoning.

This conclusion as to the general symptoms which occur in all cases of influenza, still more forcibly applies to the complications and the sequelæ.

In the complications and sequelæ due to the action of other microörganisms than the influenza-bacillus, the influenzal process affords a nidus in which germs may readily multiply; it lowers the general power of resistance to microörganisms; in some cases there probably occurs mixed infection; the bacillus of influenza or its products conferring increased activity upon certain other microörganisms with which it happens to be associated.

The morbid processes complicating or following influenza, and in which faulty chemic action is evolved is explained by (1) the general debility; (2) the special depression of the nervous system; (3) the interference with the processes of gastro-intestinal digestion; (4) interference with the chemic changes in the liver, in the blood, perhaps the spleen, and other organs, which interfere with metabolism; (5) defective action of emunctories, whereby waste-products, failing to be removed by the natural channels of elimination, accumulate within the system, and exert a toxic influence; (6) perhaps the chemic products of the influenza-bacillus itself may interfere directly with chemic transformations.

The morbid conditions due to faulty innervation —the cardiac, the gastric, and the bronchial and the intestinal disturbances—are in most cases due to poisoning, without recognizable organic change, but sometimes as a result of definite structural alteration.

The series of inflammatory and degenerative processes, the inflammations of mucous surfaces, of serous membranes, and of solid organs; those of nerves, of nerve-centers, of the membranes of the brain and cord, and the fatty degeneration of the heart, are probably due not to the bacillus but to its products.

By analogy with studies already made upon anthrax and diphtheria the conclusions may be formulated: (1) That the influenza-bacillus, which is not widely disseminated throughout the body, produces its effects by its chemic products. (2) That these chemic products may probably be of the nature of albumoses associated with an organic acid or acids, or with an alkaloid or alkaloids, which may perhaps be produced indirectly by means of a ferment secreted by the bacillus. (3) It is probable that the production of these substances takes place to some extent in the spleen, which is so often found enlarged in cases of influenza. (4) That these poisonous products act upon nervous and other tissues, producing the great variety of functional and structural changes which are met with in the later stages of the influenzal process.

In the way of prophylaxis, many facts have been ascertained which are fitted to suggest and even justify the adoption of preventive measures, although it must be admitted that the application of these measures is by no means easy.

While recent facts have thrown doubt upon the old belief in the atmospheric spread of the disease, evidence of an overwhelming force has accumulated in favor of its spread by contagion.

Epidemics do not always spread with the prevailing winds; they are independent of season and weather, are never known to travel faster than men can travel, never occur among persons so placed as to preclude communication by human agency; as a rule, appear first in each country in the ports of entry or in the frontier-towns, and in the busy capitals which were most active in intercourse with neighboring lands which had become affected; as a rule, country places remain longer free than the busy towns, even although they might be nearer the countries already invaded by the disease; the individual members of the communities who were most in contact with others were first affected; from them it spread to others with whom they were associated; among persons that were wont to congregate in crowded, and especially in ill-ventilated buildings, and where people were closely associated in public institutions, the disease came more speedily to its height and was sooner got over than when men were more secluded from one another.

Another important fact which has been made out is the shortness of the period of incubation. Sometimes the symptoms appeared almost immediately after exposure. A consideration of the brevity of the period of incubation makes clear the rapidity of the epidemic spread.

As the great majority of people are susceptible to the action of the influenzal poison, and as one attack confers no immunity to another, and as the disease often spreads from cases which are not severe and appear trifling and unimportant, its return in a community, even by contagion, ultimately surpasses what anyone could expect.

But the spread is not exclusively by direct intercourse between the sick and the sound; it is often by means of fomites. Post office and railway officials were specially apt to suffer early, and from them as centers the disease sometimes spread through the community, and these facts afford instances of the tendency the disease had to spread by letters and by parcels.

Outside the body of the healthy person the influenza-bacilli might be prevented from producing its effects, if those who have become affected with the disease could be effectively isolated. Every sneeze, and every cough probably, scatters the germs throughout the atmosphere, and if those who are affected could only be isolated the danger would greatly diminish; but isolation in a general way is impossible, and that because many cases of true influenza are so mild as to escape detection, and because even when the case is severe, infection is often spread before diagnosis is possible. But, on the other hand, now that people have ceased to regard influenza as a trifling and unimportant malady, and have come to know that it is certainly contagious, precautions have often been taken that were scarcely dreamed of in former epidemics. Infected individuals have isolated themselves, and thereby have saved their neighbors from contamination. People suffering from disease of the heart or lungs have been kept scrupulously away from the infected, and have thereby escaped what would have been to them a terrible danger. Schools have been closed, with the result of diminishing the severity of certain outbreaks, and no doubt when the next epidemic of influenza occurs, precautions of this kind will much more generally be adopted.

But even when isolation is impossible much good may be done by destruction of the sputum and of the nasal secretion. If patients expectorate into vessels containing sufficient disinfecting fluid, or into pieces of linen which are immediately thrown into the fire, innumerable quantities of noxious germs may be destroyed in each case. So, precautions as to the discharges, if once efficiently taken, would tell materially upon the epidemics.

If the bacilli discharged from the body can be thus dealt with, the question arises whether they cannot be dealt with within the bronchial tubes. If this were possible their multiplication and the development of their toxins might be prevented, and the noxious power of the sputum greatly diminished. Inhalations of many antiseptics have been recommended for this purpose; eucalyptus and menthol have been, perhaps, among the most popular. The injections into the trachea of such substances as have proved serviceable in other diseases of the respiratory tract might be tried, such as a 10 per cent. solution of menthol in olive-oil, with or without 2 per cent. of guaiacol superadded.

It is possible that during epidemics of influenza such intra-tracheal injections might confer a degree of immunity upon those exposed to the contagion.

Another question which emerges is whether any means may be discovered of conferring immunity by rendering individuals insusceptible to the action of the germs. Now the mere fact that one attack of the disease confers no immunity to subsequent attacks makes one less sanguine as to the probability of such a material being discovered, but it may, perhaps, one day be possible to supply a preventive treatment by the use of the derivatives of the specific bacillus.

Again, it would be of great service if substances were discovered by means of which the poisonous products of the bacilli would be destroyed or neutralized, and so prevent the secondary results. It is also conceivable that substances may be discovered which would act as physiologic antagonists to the influenza-toxins; but this also is in the meantime mere matter of conjecture.

The last question to be raised is whether the system generally or the organs specially affected can be so acted upon as to combat the injurious effects. There is one lesson which most people have learned from the recent epidemics, namely, that those who are taken with the disease, even in a mild form, ought not to struggle against it and go on with their work, but should yield to the malady for the time, in the hope of escaping or lessening its after-effects. When the after-effects manifest themselves, rest from bodily and mental effort is essential, and careful attention to diet, to protection from cold, to the moderate and wise use of stimulants by those who are accustomed to employ them, and of such tonics as nux vomica, quinin, arsenic, and iron, with special cardiac or other tonics when they are indicated, prove eminently beneficial.

THIRD DAY—AUGUST 2D.

The Address in Surgery was delivered by MR. J. GREIG SMITH, of Bristol, taking for his subject "The Art of the Surgeon." He pointed out that not only has the surgeon knowledge to acquire but also an art to learn. The art may be of little importance as compared with the science of surgery; there can be no dispute that it is; still, as the servant, the interpreter, occasionally even the improver of the science, it has its importance, and may be worth thinking about and worth discussing.

What is a Surgeon?

The surgeon is, first and foremost, a physician, a man trained in the laws of health and disease, in the ways of preserving health and of curing disease. In person or by proxy he must lean finally on medicine. To his medical training is superadded a special and peculiar education in the treatment of certain diseases which lend themselves to cure by the help of handicraft. The surgeon is a man who can carry the treatment of a class—a small class—of diseases farther than the physician, and that is all. The physician, on his side, goes beyond the surgeon. But both meet. In old times the surgeon was practically the slave of the physician; later on he struggled up to the dignity of being his enemy. To-day he is his equal and his helper. They join hands over the same patient, each seeking from the other some special help in healing. And herein to-day is the difficulty both of the surgeon and of the physician. Each is driven to his wits' end to meet the manifold demands made on him by the other. This is their only rivalry, a goodly and a wholesome one, leading to new victories over disease.

Amongst other arts and crafts the surgical stands alone in extraordinary breadth of its foundation on science. The painter is not expected to know the sciences of chemistry, botany, geometry, and optics, which intimately relate to his art; nor is the sculptor supposed to be familiar with geology because he works in clay and marble. Possibly both painter and sculptor would be the better for a scientific knowledge of their materials; but such knowledge is subsidiary and unessential. To the surgeon wide scientific knowledge is of prime importance; it is, indeed, essential. His range is almost coterminous with abstract science—something of all of the sciences, a good deal of a few, and everything of two or three, he must know.

Those who arrange the medical curriculum go on adding to it; where is this importation of new subjects going to stop? They go on broadening the base, and adding to the foundation; might not now some thought be given to the raising of the building?

The rolling years add to the pile of knowledge, and the burden becomes heavier to bear. To some the burden is already too heavy; others carry it easily, and even voluntarily add new weight. How to deal with the pile so that it may best minister to good is a problem always seeking solution.

Some would solve it by deliberately casting off part of the burden as being cumbersome and useless. These men say of anatomy that there is too much of it. If surgeons, they say they cut where they have to cut, and if they divide a vessel they tie it. The right kidney they find in the right loin, and the left kidney in the left loin, and they cut down till they come on it. If facts must be borne in mind till examination, there are mnemonic rhymes and cabalistic formulæ to save the labor of the brain. There is, they say, too much anatomy. They say of physiology that it is unstable and uncertain, that it is burdened with an affectation of science called by its young votaries "research;" and they affirm that the young physiologist when he becomes a physician administers a dose of castor-oil to his patient on very much the same principles as his grandmother followed when she gave a dose of the same drug to his father. Pathology also they despise. They call this the science of the "too late;" it helps us when the power of helping the patient is past. From the disintegrated remnants of the deadhouse they say one can no more work back to the beginnings of disease than from the shattered fragments of a fortification the artilleryman can work back to the powder and shot and ordnance which created the havoc.

These men are not few, and they are as honest as their opponents. Mr. Smith, with firm belief, proclaimed the very opposite. If asked of surgery "Are we to lower it so that brains may not be strained; or are we to strain our brains that surgery be raised?" he would answer unhesitatingly, "Let surgery rise if brains fall." Let the weak, or the lazy, or the impatient fall out, but do not let us lower our standard because some men cry that it is too high. It cannot be too high; it can never be high enough. The claims of surgery are such that no test of excellence can be too high for those who seek to qualify themselves for its practice.

Mr. Smith would not favor casting anything away; but he would gladly see zoölogy, and chemistry, and botany turned out of the curriculum, and placed among the preliminary studies and made part of the preliminary examination. He should like to fill their places in the curriculum with more anatomy and more physiology and more pathology. He would extend and raise education in these branches simply and solely because he firmly believed that the fullest knowledge of them goes to provide the best practice of surgical art.

In the persistent and overwhelming claims of its science, there is real danger that surgery may lose something of its art. The art of the surgeon may, for purposes of comparison, be viewed from two aspects. One is allied to the art of workers in wood and iron, and may be called mechanical. The other aspect has little of the mechanical about it, and is closely allied to a fine art. The mechanical side, the art of the application of tools, is an important but comparatively simple one. Easily learned as it is, it is still worthy of being taught. It is not, perhaps, a good thing that a surgeon should for the first time handle a saw or a chisel, or a drill, or a trephine on a living human bone; and it would be well if surgeons who have much to do with apparatus knew the qualities of the metals and other materials they

employ, and the ways of jointing, and welding, and moulding them to meet the ends desired. It would, in fact, be good for most surgeons to spend a month or two in a mechanic's shop under the severe discipline of a skilled workman. In respect of technical skill in their handling, the surgeon's tools may be placed on the level of the sculptor's spatula or chisel, or only a little higher. The chisel of the sculptor and the knife of the surgeon are mere incidents or accessories in the work to be compassed by the brain-compelled hands. Still, as accessories they have their importance; the surgeon ought to be familiar with his tools. But the surgeon is more than a mechanic; he has work to do which brings him to the level of the true artist.

The other side of surgical craft may be compared with that which produces what are known as works of art; and this side is by far the most important. Here the work of the fingers is of small moment as compared with the work of the brain. The brain is supreme, and yet in delicacy, deftness, and general preciseness of obedience to the brain's behests, the fingers and hands have great calls made on them. In painting, sculpture, or music, mere manual dexterity rarely is deficient to him who has the artistic soul; or, if there is deficiency, practice and education will do much to remove it. So in surgery, the hands rarely fail to rise to the demand the brain makes upon them if they are trained.

The highest part of the surgical art is more than handicraft; it is braincraft uttered through the fingers. It is not mere manual dexterity or cunning. In fact, mere manual cunning, being a result of routine practice which begets reflex movements, is detrimental to surgical art, which demands the widest possible scope and variety of action. The surgeon's art demands breadth and variety in manual training; the hands must have all-round capacity. By many devices and practisings he may and ought to improve their capacity; but their final and most perfect training is in the actual work.

The skill of the hand depends greatly on the sense of touch and on what has been called the muscular sense. The highest cultivation of the sense is essential to the surgeon.

The sense of touch is trained through the intellect as much as through the fingers; it is helped by comparative appeals to the other senses, and especially to sight.

There are no limits to the demands made on the surgeon's tactile powers. Touch is to the surgeon what hearing is to the physician in diagnosis, and more in treatment. In diagnosis touch tells what sight cannot; in operating in the dark depths of the body it goes where sight cannot, and sometimes it guides more truly than sight could. But always it is the intellect that interprets.

Amongst the plastic arts sculpture, perhaps, presents most points for comparison with the surgical. Each deals with the human body. The sculptor has to know the body externally in architecture, in bulk, and in outline; the surgeon has to know it in the same ways, internally as well as externally, and in sections vertical, transverse, and oblique as well. Each art demands from its votaries absolute fidelity to form; the ignorance that misplaces a tendon in a statue will lead to grief on an artery in an operation. There are similarities in their ways of working, too. The inferior sculptor, by adding here and subtracting there, by measuring and squeezing and scraping, may, after long working, make a tolerable likeness, but never a work of the highest art. The true artist goes straight to the stopping-point and then stops. What this stopping-point shall be cannot be defined, but it gives that sense of true balance between detail and mass which signifies artistic proportion. So in surgery; the surgeon-artist forms a clear conception of the work he has to do and makes straight for the ending of it. Between detail and bulk he determinedly keeps a true artistic proportion. His time is limited, and into this time he must put his best work. He wastes no time over trifles; he is very deliberate over difficulties. The most elaborate finish in both arts is visible when the technical difficulties are greatest. The clean straight strokes of a true artist are visible equally in the work of the surgeon and the sculptor.

The surgeon who is not an artist is devoid of a sense of true proportion. Where one bold cut is wanted, he will make a dainty nibbling dissection. He verifies his anatomy on the way to his work by the help of the director. He goes a little in this direction and retraces his steps; then a little in that direction and returns. He has hobbies, and he rides one or two well. One man turns the peritoneum in, the other turns it out, a third is careful to ignore it. Perhaps he gives one suture to peritoneum, one to muscle, one to fascia, and one to skin, and each suture is perhaps of a different color or a different material, so that Nature may have no chance of making a mistake. His work is not toward one finished work of art, but to the making of half a dozen clever separate studies. Like the sculptor who is good at hair, and works out every one, or the painter who is good at eyes and puts in the dots in the iris, each sacrificing the whole to the part, the inartistic surgeon lingers over his fancies, and so fails to produce finished and harmonious work. His details are not all equally balanced; some are exquisite, some are mediocre, others are bad. The whole work, the whole operation, will not be the best possible for the saving of life; it is not all round a finished work of art. Therefore it is to be condemned.

The surgeon's art has in it not only the elements of boldness, honesty, and simplicity pertaining to the sculptor's art; it leads him in some of its departments into methods of working which may fairly compare with the most delicate amongst artistic pursuits. The finest work of the surgeon makes demands on the delicacy of the fingers little, if anything, less exacting than the demands made on the fingers of the etcher or the line-engraver. The surgeon, as a painter, has to make pictures not only in life-size, but in miniature; as a sculptor he has to do not only the full figure and the medallion; his work may also be compared to that of the graver of gems.

The operative art of surgery is truly a high art;

the demands it makes on the hand, the eye, and the brain of the artist are the same for surgery and the fine arts. Surgery and fine art may indeed well be practised by the same man.

Now, of this art of surgery, where and what is the teaching? Where and who are the masters who guide and correct the young artists in their work? It may be said at once, of masters there are plenty, but they do not teach. There is no real teaching of the art of surgery in Great Britain. Here and there a favored few, house-surgeons and their assistants, are permitted to pick up what knowledge they can by looking on and by helping, but of personal guidance in the actual work on the living subject analogous to the guidance given in other arts, surgeons in theirs know nothing. They have to teach themselves by experience alone. Think what this would mean in art-training. It would mean that to paint a thousand portraits is the only way to become a first-rate portrait-painter; to model a thousand figures is to become a perfect sculptor. It means in medicine that the midwife of 5000 experiences is more to be trusted than the obstetric gold-medalist of London University, who can boast of only fifty. And note this further, the young sculptor may with impunity make and break figures to his heart's content; the young surgeon, in learning his art, is not supposed to damage or destroy human beings.

Artists, mechanics, craftsmen of all sorts, learn their work in the workshops or studios with a master to correct their faults and guide their efforts. Surgeons alone have, unassisted, to grope their way to excellence in their art. In his science the student has guidance enough in all conscience, and in his notetaking and his dressing he is sharply looked after. But he is severely left to his own devices to pick up the technics of his craft.

Is this right? That the art of surgery is teachable there can be no dispute, that it is worth teaching is still less disputable. Why, then, is it not taught?

The art can be taught in only one way, the way of teaching all the plastic arts. The young artist must while beginning the practice of his art have a master at his elbow, a master who will criticise his methods and correct them, who will guide him in the use of his hand, his eye, and his instruments, who will in the fullest sense make him his pupil and personally lead him on, step by step, toward such excellence in the art as he himself has acquired.

As a step between anatomy and surgery, the performance of operations on the dead body is of supreme value; it is indeed indispensable. It is the first step toward operative surgery, but it is not operating. For instruction in the living art of surgery, attendance in the operating-theater is of little value. The student sees little, and that little with uninstructed eyes. The student of surgery is just as likely to learn his art simply by attendance in the operating-theater as is the student of the violin to become a true artist simply by going to concerts. In both cases to learn the art the student must work at it; to attain to the highest degree of excellence he must work under a master.

If then the art of surgery is to be perfectly taught, it must be taught to the young surgeon actually operating. And here is the first difficulty. We cannot teach the art to unqualified men; students are not permitted to operate. The teaching must be begun after the student is qualified. As things are at present this is not easy. The pupil of yesterday is a colleague of to-day; when qualified he is supposed to be the equal of his teachers, and therefore above their criticism. It is difficult to imagine a skilled senior in the operating-theater calling attention to the faulty methods of his young colleague; it is impossible to conceive the former pushing the latter aside and showing him how to do it. And yet, if the living art is to be taught at all, this personal way is the only way. Why should the young surgeon more than any other artist fear tuition in the operating-theater? Possibly the presence of young students, of whom he is probably a teacher, would be a chief objection. Then, if the humility of him who truly seeks after knowledge is not forthcoming, must the young students be excluded from operations at which open instruction is given to young surgeons. And it resolves itself into this, that the master has a few qualified pupils, and is present at the operations of these few. He guides them in their work; he points out faulty methods; he advises, and, perhaps, assists; and this he does in the presence of all his pupils.

As a matter of fact, it is doubtful if the young surgeon would fear tuition in public, if such tuition were given honestly and courteously by a man whom he could look up to as a master. There is no method of education in handiwork that can surpass fair criticism of the work before compeers. The mere pointing out of faults calls attention to details which the average onlooker would fail to see. But criticism is not all fault-finding; it calls attention to excellences as well as defects. The pointing out and correcting of faults, and the praising and holding up for imitation of any special excellence in operating might well, to the advantage of all and the discomfort of a very few, form part of the routine education of the hospital operating-theater.

NEWS ITEMS.

The Vermont State Medical Society will hold its eighty-first annual meeting at Montpelier, October 11 and 12, 1894. An interesting program is in course of preparation.

"***The Nursing World***" is the name of a new "monthly journal devoted to the theory and practice of modern nursing," published at Providence, R. I., and edited by Dr. J. E. Brown.

The Cholera.—Thirteen cases of cholera, with six deaths, were reported in Maastricht in Holland, up to July 3d.

"***Health***" is the name of a new publication, which announces itself as a journal of practical hygiene.

Dr. Rudolph Matas has been elected President of the Louisiana State Medical Society.